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Management of Cancer During Pregnancy: ASCO Guideline

Alison W. Loren, MD, MSCE[1]; Christina Lacchetti, MHSc[2]; Frédéric Amant, MD, PhD[3]; Elyce H. Cardonick, MD, FACOG[4]; Lisa A. Carey, MD[5]; Nicole Christian, MD[6]; Caroline Clark, MSN, APRN, OCN[7]; Don S. Dizon, MD[8]; Melissa Henry, PhD[9]; Melissa H. Hudson, MD[10]; Julia Maués, MA[11]; Erika Peterson, MD[12]; Tatiana M. Prowell, MD[13]; Rachel Raab, MD[14]; Jane E. Rogers, PharmD[15]; Hina Saeed, MD[16]; Mikkael A. Sekeres, MD[17]; Jolyn S. Taylor, MD[15]; Katherine Van Loon, MD, MPH[18]; W. Hamish Wallace, MD[19]; Katie L. Watson, JD[20]; Siddhartha Yadav, MD[21]; and Ann H. Partridge, MD, MPH[22]

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ABSTRACT

ASCO Guidelines provide recommendations with comprehensive review and analyses of the relevant literature for each recommendation, following the guideline development process as outlined in the ASCO Guidelines Methodology Manual. ASCO Guidelines follow the ASCO Conflict of Interest Policy for Clinical Practice Guidelines.

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PURPOSE To provide guidance on the recommended management of cancer in pregnant patients.

METHODS A multidisciplinary Expert Panel convened and conducted a systematic review of the literature.

RESULTS The systematic review identified 450 eligible studies. Much of the evidence consisted of observational data, case series, and case reports.

RECOMMENDATIONS Management of cancer during pregnancy should be grounded in a values-based informed-consent process outlining maternal and fetal risks and anticipated benefits. Diagnostic evaluation should follow the as low as reasonably achievable (ALARA) principle, with timing of diagnostic studies individualized based on urgency of cancer detection, potential dangers of delay, and the balance of risks to both the pregnant patient and her embryo or fetus. Due to significant risk of harm to the developing embryo and/or fetus, systemic therapy should be deferred until the second trimester. Methotrexate, hormonal therapies, human epidermal growth factor receptor 2–targeted agents, vascular endothelial growth factor and poly (ADP-ribose) polymerase inhibitors, antibody-drug conjugates, and all cellular therapies are contraindicated during pregnancy, regardless of gestational age. For patients who wish to continue their pregnancy, delivery should be planned at or after 37 weeks, with the final chemotherapy dose scheduled 2-4 weeks before birth. Referral to psychosocial support services is essential to address emotional and practical challenges, reduce distress, and support shared decision making.

Additional information is available at www.asco.org/survivorship-guidelines.

ACCOMPANYING CONTENT

Appendix

Data Supplement

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INTRODUCTION

A new cancer diagnosis occurs in approximately one in 1,000-2,000 pregnancies. The incidence has risen in parallel with trends toward delayed childbearing and the earlier onset of some cancers.[1] Pregnancy-associated malignancies predominantly mirror those occurring in women of reproductive age: breast and cervical cancers together comprise

TARGET POPULATION AND AUDIENCE

Target Population
Pregnant people with cancer.

Target Audience
Medical oncologists, radiation oncologists, surgical oncologists, hematologists, obstetricians, radiologists, neonatologists, maternal-fetal medicine specialists, primary care clinicians, nurses, advanced practice professionals, pharmacists, and other members of the clinical care team.

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roughly 50% of cases, hematologic malignancies account for about 25%, and melanoma represents nearly 10%, with ovarian, cervical, and colorectal cancers making up smaller proportions.[2] Physiological changes of gestation (eg, hemodilution, breast engorgement, nausea, and lower back pain) may obscure early oncologic symptoms, contributing to an average diagnostic delay of 4 weeks and a higher likelihood of advanced-stage disease at presentation compared with nonpregnant patients.[3] Although advances in diagnostic imaging have improved early detection, certain modalities remain contraindicated or limited during pregnancy, further complicating timely diagnosis.

Gestational physiology can profoundly alter the pharmacokinetics and placental transfer of anticancer agents. Expanded plasma volume, increased renal clearance, and enhanced hepatic metabolism can dilute and accelerate the elimination of cytotoxics[4,5]; however, current evidence suggest that chemotherapy be dosed per usual guidelines (ie, based on actual weight).[6-10] The safety of chemotherapy during pregnancy depends largely on the timing of exposure, with generally greater risks in early pregnancy and more reassuring outcomes when treatment is given later.[11]

Optimal management of cancer in pregnancy demands a patient-centered, multidisciplinary approach. Ethical frameworks emphasize shared decision making that incorporates the pregnant individual's values, risk tolerances, and gestational age of the fetus.[12] Critical decisions, such as the timing of surgery, initiation or deferral of chemotherapy, delivery planning, and consideration of pregnancy termination, must be revisited at key gestational milestones with clear documentation and patient-centered open communication, and without compromising the quality and scope of care due to legal restrictions on abortion.[13]

The purpose of this guideline is to systematically collect and appraise the evidence published on diagnostic strategies and therapeutic interventions and to offer a series of recommendations for management of cancer during pregnancy. By integrating disease-specific epidemiology, maternal-fetal pharmacology, and ethical principles, this synthesis aims to inform consistent, evidence-based care pathways that optimize outcomes for both the pregnant patient and, if continuing the pregnancy, her embryo or fetus.

The evidence base for any set of clinical practice recommendations is built on the characteristics of the patients who participated in the underlying studies. Broad enrollment in clinical trials is essential for clinicians to assess the generalizability of trial results and understand safety and efficacy across populations. However, pregnant patients are systematically excluded from participation in oncology clinical trials.

GUIDELINE QUESTIONS

This clinical practice guideline addresses three overarching clinical questions: (1) What is the recommended diagnostic evaluation for pregnant patients with signs or symptoms of cancer? (2) For pregnant patients diagnosed with a new or recurrent cancer, what is the recommended oncologic management? (3) For pregnant patients with cancer, what is the recommended obstetrical management beyond standard obstetrical practice?

METHODS

Guideline Development Process

This systematic review-based guideline product was developed by a multidisciplinary Expert Panel, which included a patient representative and an ASCO guidelines staff member with health research methodology expertise (Appendix Table A1, online only).

The recommendations were developed using a systematic review of evidence. PubMed was searched from January 1, 2013, through May 22, 2024, for systematic reviews, randomized clinical trials, and observational studies. In the absence of trial data or cohort studies, case series, case reports, and database analyses were considered. The literature search was rerun on March 24, 2025, to identify articles published since May 2024. The reference lists of all included studies were manually reviewed to identify any additional studies, including important seminal works published before 2013 that were not captured in the initial literature search. Articles were selected for inclusion in the systematic review based on the following criteria:

1. Population: Pregnant patients with cancer, including initial diagnosis during pregnancy, worsening and/or recurrence during pregnancy, or occurrence of pregnancy during a known cancer diagnosis or treatment. Patients exclusively diagnosed and treated in the postpartum period are not considered.
2. Interventions and comparisons: Various diagnostic tests, including imaging ± contrast, biopsy, clinical laboratory tests, oncologic management options, including systemic

treatments, radiation therapy (RT), and surgery either as single treatment modality or combination treatment, and various obstetrical interventions.
3. Outcomes: Oncologic-related outcomes and adverse events, departures from standard of care, pregnancy-related outcomes, complications and adverse effects, teratogenicity, fetal and/or neonatal outcomes, and adverse effects on progeny.

Articles were excluded from the systematic review if they were (1) meeting abstracts not subsequently published in peer-reviewed journals; (2) editorials, commentaries, and news articles; and (3) published in a non-English language.

Eight full panel meetings were held, and members were asked to provide ongoing input on the guideline development protocol, assess the quality of the evidence, generate recommendations, draft content, as well as review and approve drafts during the entire development of the guideline. ASCO staff met routinely with the Expert Panel cochairs and corresponded with the Panel via e-mail to coordinate the process to completion. Ratings for the strength of the recommendation and evidence quality are provided with each recommendation, defined in Appendix Table A2. The quality of the evidence for each outcome was assessed using the Cochrane Risk of Bias tool and elements of the GRADE quality assessment and recommendations development process.[14,15] GRADE quality assessment labels (ie, high, moderate, low, very low) were assigned for each study by the project methodologist in collaboration with the Expert Panel cochairs and reviewed by the full Expert Panel. All funding for the administration of the project was provided by ASCO.

Guideline Review and Approval

The draft recommendations were released to the public for open comment from April 30, 2025, through May 13, 2025. Response categories of "Agree as written," "Agree with suggested modifications," and "Disagree. See comments" were captured for every proposed recommendation with 16 written comments received. A total of six respondents either agreed or agreed with slight modifications to 99% of the recommendations. Expert Panel members reviewed comments from all sources and determined whether to maintain original draft recommendations, revise with minor language changes, or consider major recommendation revisions.

The draft was submitted to an external reviewer with expertise in radiology. It was rated as high quality, and it was agreed it would be useful in practice. Review comments such as specifying ionizing radiation throughout, adding other radionuclide studies to avoid, replacing iodine-131 with radioactive iodine, and offering more clarity around how nuclear medicine is presented in the guideline were reviewed by the Expert Panel and integrated into the manuscript. Based on this review, revisions were made to the draft to clarify recommended actions for clinical practice. Additionally, a guideline implementability review was conducted. All changes were incorporated into the final manuscript before ASCO Evidence Based Medicine Committee (EBMC) review and approval. All ASCO guidelines are ultimately reviewed and approved by the Expert Panel and the ASCO EBMC before submission to the *Journal of Clinical Oncology* for editorial review and consideration for publication.

Guideline Updating

The ASCO Expert Panel and guidelines staff will work with cochairs to keep abreast of any substantive updates to the guideline. Based on formal review of the emerging literature, ASCO will determine the need to update. The ASCO Guidelines Methodology Manual (available at www.asco.org/guideline-methodology) provides additional information about the guideline update process. This is the most recent information as of the publication date.

RESULTS

Characteristics of Studies Identified in the Literature Search

A total of 1,096 studies were identified in the initial literature search. The refreshed literature search identified an additional 81 studies, plus another 66 older studies were found from reviewing reference lists. After applying the eligibility criteria, 450 studies remained, forming the evidentiary basis for the guideline recommendations.

Evidence Quality Assessment

The current evidence informing recommendations for the diagnosis, oncologic management, and obstetrical management of pregnant patients with cancer is mostly based on retrospective observational studies, case series, and individual case reports. While these study designs offer valuable insights into a relatively rare and complex patient population, they are nevertheless inherently limited by potential bias, small sample sizes, and heterogeneity in study populations and treatment protocols and may not fully capture the nuances of long-term maternal and fetal outcomes. Furthermore, existing evidence often fails to adequately address effects that are scientifically uncertain and potentially too subtle to be clinically detectable. Although overt adverse outcomes such as significant maternal morbidity, fetal growth restrictions (FGRs), or congenital anomalies at birth are well documented, more subtle long-term effects, such as neurodevelopmental differences or endocrine alterations, may remain undetected in studies with limited follow-up periods. This gap underscores the need for cautious interpretation of the data, as the absence of detectable effects does not necessarily equate to the absence of any impact. Despite these limitations, the evidentiary base provides valuable real-world data that can guide clinical practice, although results should be interpreted with caution considering these inherent methodological limitations. Refer to Appendix Table A2 for definitions for the quality of

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the evidence, and the Methodology Manual for more information.

RECOMMENDATIONS

All recommendations are available in Table 1, and Figures 1-5 show the recommendations as algorithms.

DIAGNOSTIC EVALUATION

Literature Review and Analysis

Evidence on the feasibility, effectiveness, and safety of various approaches used to diagnose and stage cancer in pregnant people, including imaging, serum tumor markers, and cytological evaluation, was identified in the systematic review of the literature. A total of 72 papers met the inclusion criteria and form the evidentiary base for current best practices for evaluating cancer in this unique population.[8,9,16-25,26-50,51-85] The quality of evidence supporting diagnostic testing for malignancy in pregnant patients is generally low, primarily due to reliance on case reports, case series, and expert opinion. Evidence quality was upgraded to moderate when findings were consistent across multiple studies, and when diagnostic approaches demonstrated reproducible accuracy and/or safety profiles in pregnant populations across diverse clinical settings.

Imaging and General Safety Considerations

Two primary categories of radiation effects are described in the literature: deterministic and stochastic. Deterministic effects are dose-dependent and result from radiation exposure exceeding established thresholds, with potential outcomes including pregnancy loss, fetal malformations, growth restriction, and neurodevelopmental impairment.[16] While general dose thresholds have been proposed, the exact values remain uncertain due to the paucity of robust human data.[16] In contrast, the severity of stochastic effects does not depend on the radiation dose. Instead, these effects can theoretically occur at any level of exposure, with the probability of occurrence increasing as the dose rises.[16]

Diagnostic imaging involving ionizing radiation may be required during pregnancy, necessitating a careful evaluation of the safest and most suitable imaging modality that provides essential information while minimizing risks to both the pregnant patient and her embryo or fetus.[17,18] All ionizing radiation procedures should be conducted in accordance with the "as low as reasonably achievable" (ALARA) principle,[19] as there is no known threshold for stochastic effects of radiation. To reduce ionizing radiation exposure in pregnant patients, unnecessary imaging should be avoided, and alternative modalities that do not involve ionizing radiation should be used whenever feasible and suitable.[20]

Observational studies and expert consensus documents consistently report that ionizing radiation doses from most standard diagnostic procedures fall well below levels associated with deterministic fetal harm.[17,21] Doses under 50 mGy are not associated with increased risks of congenital anomalies or pregnancy loss.[20,22,23] While exposures between 50 and 100 mGy are more difficult to evaluate, available data suggest these levels are also unlikely to result in measurable fetal effects.[16,21]

The impact of ionizing radiation on the embryo or fetus varies by gestational age (Table 2). During the preimplantation stage (0-2 weeks' gestation), exposures above threshold levels may result in pregnancy loss, following the "all-or-none" phenomenon.[24] During organogenesis (2-8 weeks), embryos are particularly vulnerable to structural malformations, especially of the central nervous system.[25] However, mutagenic effects are difficult to detect, and while radiation may slightly increase genetic mutation rates, no unique mutations have been attributed to ionizing radiation.[16] In the second trimester, fetal sensitivity declines, although growth restriction and neurodevelopmental effects have been reported following higher exposures.[16] In the third trimester, fetuses are least sensitive to deterministic effects.[25]

Most diagnostic imaging procedures deliver fetal doses well below the 50 mGy threshold (Table 2). Accordingly, the available evidence does not support deferring clinically indicated imaging due to concerns about fetal ionizing radiation exposure.[17,21] Nevertheless, attention to dose minimization and use of nonionizing alternatives (eg, ultrasound, magnetic resonance imaging [MRI]) remains common practice where feasible.

The use of gonadal and fetal shielding has been examined in recent literature.[26] Position statements advising against their routine use from multiple professional organizations, including the American Association of Physicists in Medicine,[27] National Council on Radiation Protection and Measurements,[28] and Canadian Association of Radiologists,[29] report that shielding provides minimal benefit in diagnostic imaging and may inadvertently increase scatter and therefore radiation exposure to the embryo or fetus.[26]

Although limited in number, studies addressing counseling and obtaining informed consent for imaging procedures involving ionizing radiation emphasize the importance of quantifying fetal dose, contextualizing the associated risks, and clearly articulating the potential benefits of imaging when obtaining informed consent.[16,17,81]

Ultrasound

When possible, ultrasound should be the primary diagnostic tool for cancer detection in pregnancy due to its favorable safety profile.[23,30] It is a first-line modality for breast cancer and ovarian masses.[31] In studies of breast

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TABLE 1. Summary of All Recommendations

Clinical Question	Recommendation
General Note. The following recommendations (strong or conditional) and terminology (Data Supplement) represent reasonable options for patients depending on clinical circumstances and in the context of individual patient preferences. Recommended care should be accessible to patients whenever possible	
General management principles	1.1. For pregnant patients with cancer, multidisciplinary teams including hematologists/oncologists, obstetricians, radiologists, neonatologists, maternal-fetal medicine specialists, primary care clinicians, nurses, advanced practice providers, and pharmacists should collaborate frequently to develop and adjust individualized treatment plans based on the patient's condition and response to treatment. (Evidence quality: Low; Strength of recommendation: Strong)
	1.2. Clinicians should engage in comprehensive multidisciplinary informed consent discussions with pregnant patients with cancer and their caregiver(s) before initiating or continuing any procedure or therapy. These discussions should clearly outline known risks to the patient and to the embryo or fetus (ie, using clinical and animal data available in the drug label), potential benefits, and treatment timelines. Patients should be informed of the risks associated with both pursuing and delaying cancer-directed therapy, as well as the right to change their minds at any point, understanding that doing so may alter risks, benefits, and available treatment options. (Evidence quality: Low; Strength of recommendation: Strong)
	1.3. Clinicians should prioritize autonomy and support informed decision making for pregnant patients with cancer, including whether the person decides to end or to continue their pregnancy while undergoing treatment. (Evidence quality: Low; Strength of recommendation: Strong)
	Note for Recommendation 1.3: Cancer may result in medical emergencies that require immediate initiation of cancer-directed therapy. When these emergencies occur, termination of the pregnancy may be necessary to prevent the pregnant patient's death or to mitigate the risk of death. Terminating pregnancy may also be necessary to avert serious permanent impairment to a pregnant patient's life-sustaining organ, or a serious risk of a substantial, irreversible, and/or life-threatening physical impairment of a major bodily function. Lastly, pregnancy termination may be necessary to allow optimal cancer treatment.
	1.4. For patient and clinician support in complex or challenging decision making about cancer management during pregnancy, clinicians should involve medical ethicists and, when appropriate, legal counsel. (Evidence quality: Low; Strength of recommendation: Strong)
	1.5. When managing cancer during pregnancy, clinicians should consider fetal viability in the context of maternal health and cancer prognosis. Maternal survival is essential to fetal survival, particularly in early gestation, and treatment should prioritize maternal health. Patients should be counseled accordingly, especially if the fetus has not yet reached viability. (Evidence quality: Low; Strength of recommendation: Strong)
What is the recommended diagnostic evaluation for pregnant patients with signs or symptoms of cancer?	General note for diagnostic evaluation: When proceeding with diagnostic evaluation or staging in pregnant patients with suspected or confirmed cancer, clinicians must balance the urgency of an accurate diagnosis with the safety of both the patient and her fetus. This requires a multidisciplinary approach that considers the risks of diagnostic procedures, the gestational age, and the potential impact of delayed diagnosis or therapy, ensuring that risks and benefits are clearly communicated to the patient. Informed consent, reference materials (ie, label, literature), and patient values and preferences are central to decision making.
	2.1. For pregnant patients with a palpable mass or signs or symptoms suspicious for, but without confirmation of malignancy, clinicians should immediately refer for diagnostic imaging with clear communication to the imaging facility that the patient is pregnant to ensure appropriate imaging protocols. (Evidence quality: Low; Strength of recommendation: Strong)
	The following recommendations (2.2 to 2.17) apply to pregnant patients requiring diagnostic imaging for malignancy.
	2.2. Ionizing radiation-based procedures should only be used when clinically necessary, following the "as low as reasonably achievable" (ALARA) principle to minimize fetal exposure. (Evidence quality: Low; Strength of recommendation: Strong)
	Note for Recommendation 2.2: When obtaining consent for imaging procedures involving ionizing radiation, clinicians should inform pregnant patients with cancer about the benefits and risks of the procedure, as well as the risks associated with not proceeding.
	2.3. Clinicians should order ultrasound as the first-line imaging tool whenever possible due to its safety and absence of radiation exposure. (Evidence quality: Moderate; Strength of recommendation: Strong)
	2.4. Clinicians may use MRI without contrast when further staging or clarification is necessary. (Evidence quality: Moderate; Strength of recommendation: Strong)
	2.5. Clinicians should avoid routine use of gonadal and fetal shielding devices during X-ray–based diagnostic imaging, as they provide minimal benefit, can reduce radiological image quality, and may increase scatter, potentially exposing embryo or fetus to higher radiation levels. (Evidence quality: Moderate; Strength of recommendation: Strong)
	2.6. Clinicians may use X-rays of the head and neck, chest, or extremities when clinically indicated, as fetal radiation exposure is minimal. (Evidence quality: Moderate; Strength of recommendation: Strong)
	2.7. Clinicians may use mammography as an adjunct to ultrasound in pregnant patients with suspicious breast findings. When mammography is performed, bilateral imaging is recommended as part of the diagnostic workup to avoid missing bilateral disease. (Evidence quality: Moderate; Strength of recommendation: Strong)
	2.8. For pregnant patients requiring advanced imaging for malignancy, clinicians should avoid abdominal CT, abdominal X-ray, PET-CT, bone scintigraphy, and other radionuclide studies unless essential for diagnosis, staging, and/or treatment planning. If required or indicated, timing should be individualized considering the urgency of diagnosis, the potential impact of delayed cancer detection or inaccurate staging, and the risks to both the patient and her embryo or fetus. Dose-reduction techniques should be applied to reduce fetal exposure. (Evidence quality: Low; Strength of recommendation: Strong)
	2.9. Clinicians should avoid GBCAs unless absolutely necessary due to potential fetal exposure and risks of neonatal rheumatic and inflammatory conditions or stillbirth. If there are no safer alternatives and GBCA use is unavoidable, clinicians should use the lowest possible dose. (Evidence quality: Low; Strength of recommendation: Strong)

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TABLE 1. Summary of All Recommendations (continued)

Clinical Question	Recommendation
	2.10. For pregnant patients requiring iodinated contrast for imaging, clinicians should be aware of the risk of neonatal hypothyroidism. When no safer alternatives are available and iodinated contrast is unavoidable, its use should be carefully evaluated through transdisciplinary collaboration. Neonates exposed to iodinated contrast in utero should have thyroid function evaluated through standard newborn screening for congenital hypothyroidism at birth. (Evidence quality: Low; Strength of recommendation: Strong)
	2.11. For pregnant patients requiring imaging for thyroid cancer, radioactive iodine is contraindicated. Clinicians should use ultrasound as the first-line imaging tool. (Evidence quality: Moderate; Strength of recommendation: Strong)
	2.12. For pregnant patients with suspected malignancy, clinicians should not rely solely on serum tumor markers for cancer diagnosis, as physiological changes during pregnancy can alter some marker levels and reduce sensitivity and specificity. When tumor markers are tested, results should be interpreted with caution and in conjunction with other assessments. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	2.13. When biopsy is planned, clinicians should prioritize core needle biopsy or excisional biopsy over fine-needle aspiration, to preserve tissue architecture and reduce diagnostic delays. This is an important consideration in all patients, but especially in pregnancy, where timely diagnosis can be critical for optimizing maternal and fetal outcomes. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	2.14. For pregnant patients who would benefit from sentinel lymph node evaluation, clinicians should perform SLNB, with technetium-99m (Tc-99) preferred over blue dye to reduce the risk of maternal anaphylaxis. When clinically appropriate, a 1-day, low-dose Tc-99 protocol can be used to minimize fetal radiation exposure. (Evidence quality: Moderate; Strength of recommendation: Strong)
	2.15. For pregnant patients with suspected cervical cancer, clinicians may perform colposcopy during any trimester when necessary to establish a diagnosis. Endocervical curettage should be avoided to reduce preterm labor risks. (Evidence quality: Low; Strength of recommendation: Conditional)
	2.16. For pregnant patients requiring GI endoscopy for suspected cancer, clinicians may perform endoscopic procedures, with transdisciplinary discussions about risk and timing. (Evidence quality: Low; Strength of recommendation: Conditional)
	2.17. For pregnant patients with abnormal noninvasive prenatal screening results that may be suggestive of possible cancer, clinicians should evaluate with appropriate workup. (Evidence quality: Low; Strength of recommendation: Conditional)
	Note for Recommendation 2.17: Given the need for further research on the impact of these forms of early cancer detection methods on patient outcomes and treatment strategies, clinicians should prioritize cautious interpretation of findings, multidisciplinary evaluation, and informed patient counseling.
For pregnant patients diagnosed with a new or recurrent cancer, what is the recommended oncologic management?	3.1. Treatment should be individualized based on cancer type, goals of therapy, gestational age, maternal and fetal risks, and patient autonomy including preference regarding treatment options, and pregnancy continuation or termination. (Evidence quality: High; Strength of recommendation: Strong)
	3.2. For pregnant patients with cancer requiring systemic therapy, if the patient intends to continue the pregnancy, clinicians should try to avoid administering conventional cytotoxic chemotherapy during the first trimester due to high teratogenic or abortifacient risks. (Evidence quality: Moderate; Strength of recommendation: Strong)
	Note for Recommendation 3.2: When obtaining consent for cancer-directed therapies, clinicians should inform pregnant patients with cancer about the benefits and risks of these therapies to both the patient and her embryo or fetus, as well as the risks associated with not proceeding with treatment.
	3.3. Despite clear guidance that individuals undergoing cancer treatment should use highly effective contraception, pregnancies may still occur. In such cases, acknowledging the limitations of existing evidence and the uncertainty regarding treatment-related harms in many settings, clinicians should engage in timely, individualized discussions that address the risks of in utero exposure to cancer treatment, including fetal harm and pregnancy complications; the risks to the pregnant patient of withholding further cancer treatment including potential reduction in likelihood of cancer response and/or cure; and the consideration of pregnancy termination. (Evidence quality: Low; Strength of recommendation: Strong)
	Note for Recommendation 3.3: The recommendations for cancer-directed therapies in pregnant patients are based primarily on observational data and case series often with small sample sizes. As a result, evidence regarding the safety of specific treatments during pregnancy remains limited. Clinicians should proceed with caution when making treatment decisions, recognizing that "caution" entails a thorough risk-benefit assessment for both the patient and her embryo or fetus. This may include multidisciplinary consultation, individualized risk assessment, timing considerations, drug and dose selection and duration, fetal monitoring, and shared decision making. In general, the ideal treatment in pregnant patients is the same as in those not pregnant and dosing is based on actual weight; however, clinicians may need to adjust the therapeutic plan and should refer to prescribing information in the most up-to-date FDA labels.
	The following recommendations (3.4 to 3.34) apply to pregnant patients with cancer who wish to continue their pregnancy. Each recommendation aims to balance maternal treatment needs with fetal safety. The recommendations regarding antineoplastic drugs presented herein are based on the best available evidence at the time of guideline development. This list is not exhaustive and may evolve as new data emerge.
	Alkylating agents
	3.4. Clinicians may administer alkylating agents such as cyclophosphamide, ifosfamide, and dacarbazine in the second and third trimesters. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	Antimetabolites
	3.5. Clinicians should not administer methotrexate in any trimester due to its teratogenic and abortifacient effects. Alternative treatments should be offered, or therapy should be delayed until after delivery. (Evidence quality: Low; Strength of recommendation: Strong)

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TABLE 1. Summary of All Recommendations (continued)

Clinical Question	Recommendation
	3.6. Before initiating fluoropyrimidine chemotherapy such as 5-FU and capecitabine in pregnant patients with cancer, the Panel recommends genetic testing to identify those with DPD deficiency due to genetic variations in the *DPYD* gene, to mitigate the risk of serious adverse reactions. (Evidence quality: Low; Strength of recommendation: Conditional)
	3.7. Clinicians may administer 5-FU and capecitabine in the second and third trimesters, with *DPYD* genotype-guided treatment modification when indicated. Gemcitabine may also be administered in the second and third trimesters. (Evidence quality: Low-Moderate; Strength of recommendation: Conditional)
	Note for Recommendation 3.7: Clinicians should be aware of the signs and symptoms associated with adverse reactions due to DPD deficiency, including severe mucositis, diarrhea, neutropenia, and neurotoxicity, and advise patients to immediately contact their oncology clinician if these occur.
	Platinum agents
	3.8. Clinicians may administer platinum agents such as carboplatin, cisplatin, and oxaliplatin in the second and third trimesters. Carboplatin is preferred over cisplatin due to lower fetal ototoxicity risks when compared with cisplatin. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	Note for Recommendation 3.8: See Recommendation 4.9 for postnatal auditory screening for platinum-exposed infants.
	Anthracyclines
	3.9. Clinicians may administer anthracyclines such as doxorubicin, epirubicin, and daunorubicin in the second and third trimesters. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	3.10. Clinicians should avoid the use of idarubicin in all trimesters, due to risk of congenital malformations, fetal cardiotoxicity, and pregnancy loss. If no other anthracycline is felt to be an appropriate substitute, the patient should be counseled about limited safety data for using idarubicin in pregnancy. (Evidence quality: Low; Strength of recommendation: Conditional)
	Topoisomerase inhibitors
	3.11. Clinicians may administer topoisomerase inhibitors such as irinotecan and etoposide in the second and third trimesters. (Evidence quality: Low; Strength of recommendation: Conditional)
	Vinca alkaloids
	3.12. Clinicians may administer vinca alkaloids such as vincristine, vinblastine, and vinorelbine in the second and third trimesters. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	Taxanes
	3.13. Clinicians may administer taxanes such as paclitaxel and docetaxel in the second and third trimesters. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	Hormonal therapy
	3.14. Clinicians should not administer tamoxifen, aromatase inhibitors, or GnRH agonists in any trimester due to risks of teratogenicity, fetal development complications, and spontaneous abortion. Alternative antineoplastic therapy should be offered, or therapy should be delayed until after delivery. (Evidence quality: Moderate; Strength of recommendation: Strong)
	HER2-targeted therapies
	3.15. Clinicians should not administer HER2-targeted therapies, such as trastuzumab, pertuzumab, lapatinib, and neratinib in any trimester due to risks of oligohydramnios, IUGR, and need for more safety data. Therapy should be delayed until after delivery. (Evidence quality: Moderate; Strength of recommendation: Strong)
	VEGF or VEGFR-targeted therapies
	3.16. Clinicians should not administer VEGF inhibitors such as bevacizumab, ramucirumab, or aflibercept in any trimester due to risks of IUGR, miscarriage, and maternal vascular complications. Alternative treatments should be offered, or therapy should be delayed until after delivery. (Evidence quality: Low; Strength of recommendation: Strong)
	EGFR-targeted therapies
	3.17. Clinicians should avoid cetuximab use in all trimesters due to a lack of experience in pregnancy and need for more safety data. If treatment cannot be safely deferred until the postpartum period, cautious use and close monitoring is advised. (Evidence quality: Low; Strength of recommendation: Conditional)
	3.18. Clinicians may administer EGFR-targeted TKIs such as erlotinib, gefitinib, afatinib, or osimertinib in the second and third trimesters. (Evidence quality: Low; Strength of recommendation: Conditional)
	ALK-targeted therapies
	3.19. Clinicians should avoid ALK-targeted therapies such as crizotinib and alectinib in all trimesters due to limited reports of use in pregnancy and need for more safety data. If treatment cannot be safely deferred until the postpartum period, cautious use after first trimester and close monitoring is advised. (Evidence quality: Low; Strength of recommendation: Conditional)
	ABL tyrosine kinase inhibitors
	3.20. Clinicians may administer ABL-targeted TKIs such as imatinib and nilotinib in the second and third trimesters. (Evidence quality: Low; Strength of recommendation: Conditional)
	3.21. Clinicians should not administer dasatinib in any trimester due to risks of teratogenicity, growth restrictions, and spontaneous abortion. Alternative treatments should be offered, or therapy should be delayed until after delivery. (Evidence quality: Low; Strength of recommendation: Strong)

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TABLE 1. Summary of All Recommendations (continued)

Clinical Question	Recommendation
	CD20-targeted therapies
	3.22. Clinicians may administer CD20-targeted agents such as rituximab in the second and third trimesters with close monitoring for fetal development and neonatal hematologic abnormalities. (Evidence quality: Low; Strength of recommendation: Conditional)
	MEK and RAF inhibitor therapies
	3.23. Clinicians should not administer MEK inhibitors such as trametinib in any trimester due to risks of teratogenicity, growth restriction, and neonatal toxicity. Alternative treatments should be offered, or therapy should be delayed until after delivery. (Evidence quality: Low; Strength of recommendation: Strong)
	3.24. Clinicians may administer BRAF-targeted TKIs such as vemurafenib in the second and third trimesters. (Evidence quality: Low; Strength of recommendation: Conditional)
	Antibody-drug conjugates
	3.25. Clinicians should generally avoid antibody-drug conjugates such as trastuzumab emtansine, trastuzumab deruxtecan, sacituzumab govitecan, mirvetuximab soravtansine, tisotumab vedotin, enfortumab vedotin, datopotamab deruxtecan, brentuximab vedotin, etc, during all trimesters of pregnancy due to concerns for fetal toxicity based on mechanism of action and lack of safety data. (Evidence quality: Low; Strength of recommendation: Strong)
	Immune checkpoint inhibitors (CTLA-4 and PD-1/PD-L1 inhibitors)
	3.26. Clinicians should avoid the use of checkpoint inhibitors such ipilimumab, nivolumab, and pembrolizumab in all trimesters due to potential fetal immune system disruption, fetal autoimmune complications, and increased risk of miscarriage, stillbirth, and preterm labor. If use is essential, restrict to 12-32 weeks of gestation. (Evidence quality: Low; Strength of recommendation: Conditional)
	Note for Recommendation 3.26: The transfer of monoclonal antibodies across the placenta increases during the second and third trimesters of pregnancy. As such, it is preferable to avoid their use after 32 weeks of gestation.
	Interferon-α
	3.27. Clinicians may administer interferon-α for chronic myeloid leukemia in any trimester. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	PARP inhibitors
	3.28. Clinicians should not administer PARP inhibitors in any trimester due to lack of human data and findings from animal studies indicating risks of teratogenicity, embryo-fetal toxicity, and fetal death. Alternative treatments should be offered, or therapy should be delayed until after delivery. (Evidence quality: Very low; Strength of recommendation: Strong)
	Other antineoplastic therapies
	3.29. Clinicians should not use cellular therapies, hematopoietic cell transplant, and radiopharmaceuticals due to insufficient safety evidence. Alternative treatments should be offered, or therapy should be delayed until after delivery. (Evidence quality: Low; Strength of recommendation: Strong)
	Radiation therapy
	3.30. If radiation therapy is required for pregnant patients with cancer, the radiation oncology team should ensure cumulative fetal exposure remains below 100 mGy and use appropriate abdominal shielding to reduce fetal exposure. Abdominal and pelvic radiation should be avoided to minimize fetal risks. (Evidence quality: Moderate; Strength of recommendation: Strong)
	Surgery
	3.31. Surgeons should perform surgery on pregnant patients with cancer when clinically indicated, implementing strategies to optimize maternal and fetal outcomes. To minimize risks, the surgical team should prevent maternal hypoxia, avoid supine positioning after 20 weeks' gestation, use regional anesthesia when feasible, and coordinate with a multidisciplinary team to guide perioperative management. (Evidence quality: Moderate; Strength of recommendation: Strong)
	Note for Recommendation 3.32: While surgery in the second trimester carries lower risk of spontaneous miscarriage or preterm labor, surgery can be performed safely at any gestational age with appropriate precautions.
	Supportive care
	3.32. Clinicians may offer antiemetics such as ondansetron or metoclopramide for treatment-induced nausea and vomiting. Use of other antiemetic agents such as prochlorperazine, olanzapine, and NK1 receptor antagonists should be guided by multidisciplinary consultation, as efficacy for treatment-induced nausea and vomiting and/or fetal safety data remain limited. Glucocorticoids, preferably prednisolone or methylprednisolone, may be used when needed. (Evidence quality: Moderate; Strength of recommendation: Strong)
	3.33. Clinicians may offer G-CSF to reduce the risk of febrile neutropenia when clinically indicated, such as with myelosuppressive chemotherapy. Decisions should be based on individual risk factors, gestational age, and benefits versus risks. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	3.34. Clinicians may administer broad-spectrum antimicrobials as indicated for sepsis in pregnant patients with cancer. (Evidence quality: Moderate; Strength of recommendation: Strong)

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TABLE 1. Summary of All Recommendations (continued)

Clinical Question	Recommendation
For pregnant patients with cancer, what is the recommended obstetrical management?	4.1. Obstetricians and oncologists should collaborate closely to plan delivery at or after 37 weeks of gestation to minimize prematurity risks, unless maternal or fetal health conditions require earlier intervention. (Evidence quality: Moderate; Strength of recommendation: Strong)
	4.2. Clinicians should plan to administer the last chemotherapy dose 2-4 weeks, or one complete cycle, prior to delivery, to minimize the risks of maternal and neonatal myelosuppression at delivery. (Evidence quality: Moderate; Strength of recommendation: Strong)
	4.3. Clinicians should prioritize vaginal delivery, as per standard practice and considerations, unless standard obstetric conditions or malignancies such as cervical or vulvar cancer necessitate cesarean section to optimize maternal and neonatal outcomes. (Evidence quality: Moderate; Strength of recommendation: Strong)
	4.4. For pregnant patients undergoing cancer treatment, clinicians should schedule fetal monitoring that includes at least every three-to-four-week ultrasounds starting at 22-24 weeks to assess fetal growth, amniotic fluid levels, and placental function. (Evidence quality: Moderate; Strength of recommendation: Strong)
	4.5. Clinicians may administer a single course of antenatal corticosteroids to promote fetal lung maturation for pregnant patients with delivery planned or imminent prior to 37 weeks. (Evidence quality: Moderate; Strength of recommendation: Strong)
	4.6. For postpartum patients with cancer, clinicians may initiate VTE prophylaxis with low molecular weight heparin for at least 6 weeks to reduce clotting risks. Decisions regarding VTE prophylaxis should be individualized based on factors such as a history of VTE, cancer type and stage, obstetric mode of delivery, immobility, ongoing cancer therapy, and benefits versus risks. (Evidence quality: Moderate; Strength of recommendation: Conditional)
	4.7. A histological evaluation of the placenta is recommended immediately after delivery in pregnant patients with a cancer diagnosis to guide oncological evaluation in the neonate. If placental metastases are detected, consult with a neonatologist for follow-up of neonate. (Evidence quality: Low; Strength of recommendation: Strong)
	4.8. For postpartum patients immediately undergoing chemotherapy, hormonal, or targeted therapy, clinicians should discourage breastfeeding and offer counseling on alternative feeding methods. (Evidence quality: Moderate; Strength of recommendation: Strong)
	4.9. For neonates exposed to in utero cancer therapies, pediatricians should monitor for therapy-related complications to ensure early detection and intervention. This may include, but is not limited to, baseline clinical laboratory tests (complete blood count, liver function tests, kidney function) for chemotherapy or targeted therapy exposure, auditory screening for exposure to platinum agents, and fetal thyroid monitoring for exposure to iodinated contrast enhanced CT imaging. (Evidence quality: Moderate; Strength of recommendation: Strong)
Psychological and social support	5.1. For pregnant patients with cancer, clinicians should refer for psychosocial support to address emotional and social challenges, to help alleviate distress and to facilitate decision making. (Evidence quality: Moderate; Strength of recommendation: Strong)
	5.2. For pregnant patients with cancer, their caregivers, and their families, clinicians should engage a social worker or patient navigator to provide practical support, assist with care coordination, help navigate health care systems and access community resources and peer support groups. Psychosocially complex cases should be referred to a psychologist. (Evidence quality: Low; Strength of recommendation: Strong)

NOTE. The strength of the recommendation is defined as follows: Strong: In recommendations for an intervention, the desirable effects of an intervention outweigh its undesirable effects. In recommendations against an intervention, the undesirable effects of an intervention outweigh its desirable effects. All or almost all informed people would make the recommended choice for or against an intervention. Conditional: In recommendations for an intervention, the desirable effects probably outweigh the undesirable effects, but appreciable uncertainty exists. In recommendations against an intervention, the undesirable effects probably outweigh the desirable effects, but appreciable uncertainty exists. Most informed people would choose the recommended course of action, but a substantial number would not.

Abbreviations: ABL, Abelson tyrosine kinase; ALK, anaplastic lymphoma kinase; BRAF, v-Raf murine sarcoma viral oncogene homolog B1; CD20, cluster of differentiation 20; CT, computed tomography; CTLA-4; cytotoxic T-lymphocyte antigen 4; DPD, dihydropyrimidine dehydrogenase; EGFR, epidermal growth factor receptor; FDA, US Food and Drug Administration; GBCAs, gadolinium-based contrast agents; G-CSF, granulocyte colony-stimulating factor; GnRH, gonadotropin-releasing hormone; HER2, human epidermal growth factor receptor 2; MEK, mitogen-activated protein kinase; NK1, neurokinin-1; PARP, poly (ADP-ribose) polymerase; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PET, positron emission tomography; SLNB, sentinel lymph node biopsy; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor; VEGFR, vascular endothelial growth factor receptor; VTE, venous thromboembolism.

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cancer during pregnancy (PrBC), ultrasound demonstrated high sensitivity, particularly in the presence of a palpable mass.[32-34] However, some caution is warranted, as PrBC may present with features typically associated with benign lesions, such as parallel orientation, smooth margins, and posterior acoustic enhancement.[23,35] Furthermore, ultrasound can be limited by factors such as body habitus, fetal positioning, and maternal abdominal distention.[36] These limitations may necessitate the use of additional imaging modalities when further clarification or staging is required.[36]

In observational studies, ultrasound in combination with diffusion tensor imaging (DTI) improved lesion characterization, particularly for breast cancer in pregnancy, and facilitated assessment in situations where mammography was limited or contraindicated.[37,38]

In a prospective cohort of 236 pregnant individuals with ovarian masses, three scoring systems, Sassone, Lerner, and IOTA, were compared for malignancy prediction.[39] The Sassone system demonstrated the highest predictive accuracy (AUC = 0.83). A combined scoring model incorporating

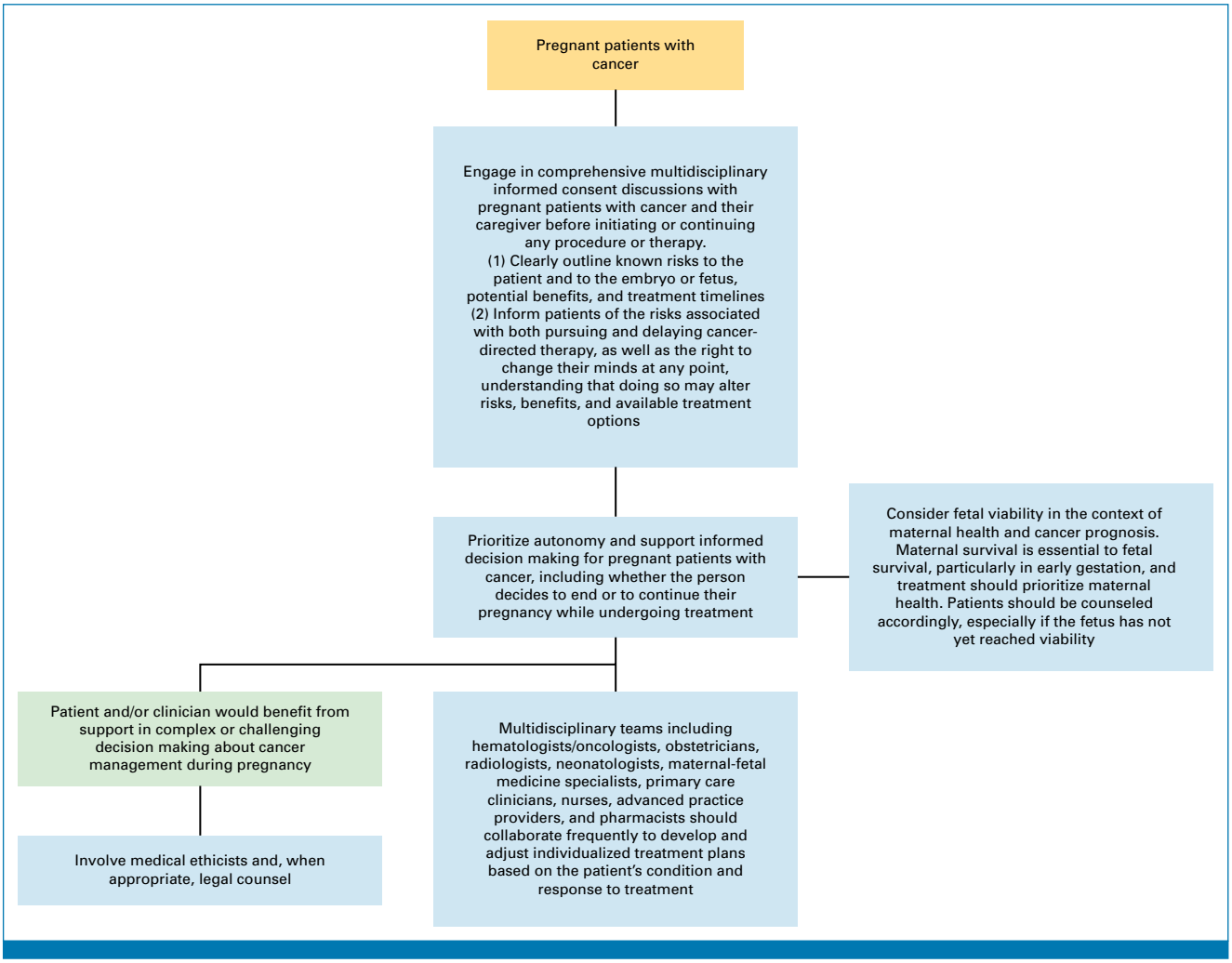

FIG 1. General management for pregnant patients with cancer algorithm.

six ultrasound parameters achieved improved performance (AUC = 0.88).[39]

Mammography

Studies assessing fetal exposure from mammography report negligible fetal ionizing radiation doses (<0.03 mGy), well below deterministic risk thresholds.[23,30] Mammography has slightly lower sensitivity (between 72% and 100%) for PrBC detection compared with breast ultrasound.[23,32] Increased breast density and change in fat and water content in pregnant patients can hinder mammography accuracy.[30] Therefore, although diagnostic mammography is not typically recommended as the initial test for palpable masses, evidence suggests it may play a supplementary role alongside ultrasound. If ultrasound does not reveal the cause of a palpable mass, mammography can help identify malignant calcifications or structural changes. When ultrasound shows suspicious findings, bilateral mammography is advised to check for additional concerning features, particularly microcalcifications that may not be detected by ultrasound.[23]

X-Ray

Data from multiple observational studies indicate that diagnostic X-rays of the head, neck, chest, and extremities result in fetal exposures <0.01 mGy and have not been associated with adverse fetal outcomes in reported cases.[40,41]

Magnetic Resonance Imaging

When ultrasound does not provide sufficient detail for a thorough assessment, MRI, which is free from ionizing radiation, offers a highly effective alternative, particularly for cancer staging.[36,40] Cohort and case-control studies evaluating the effects of exposure to routine MRI without contrast during pregnancy on adverse fetal and neonatal outcomes have found no significant differences in birth weight, motor functioning, social or neurological development, or neonatal hearing between infants exposed to MRI in utero and those who were not.[42,43,79] Current MRI safety guidelines recommend using the lowest possible magnetic field strength, with some studies advising against exceeding 1.5 T for pregnant patients.[36] Proper patient positioning with

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TABLE 2. Gestational Age, Radiation Dose, and Potential Effects

Conception Age	Radiation Dose, mGy	Potential Effect
Preimplantation 1-2 weeks	<50	No significant effects
	50-100	Pregnancy loss or no consequences ("all or none" phenomenon)
	>100	Pregnancy loss or no consequences ("all or none" phenomenon)
Organogenesis 3-8 weeks	<50	No significant effects
	50-100	Potential effects remain scientifically uncertain and likely too subtle to be detected clinically
	>100	Risk of congenital malformations (eg, CNS defects) during organogenesis; risk of growth restriction (at 200-250 mGy)
9-15 weeks	<50	No significant effects
	50-100	Potential effects are not well established but elevated risk of intellectual disability due to period of rapid neuronal development
	>100	Risk of developmental delays, intellectual disability, CNS malformations, microcephaly
16-25 weeks	<50	No significant effects
	50-100	Stochastic effects possible[a]; lower risk of severe outcomes compared with earlier stages
	>100	Risk of intellectual disability; potential developmental disturbances
>25 weeks	<50	No significant effects
	50-100	Slight increase in stochastic effects[a] (eg, childhood cancer)
	>100	Growth restriction, organ malformations possible at very high doses

NOTE: Adopted from the American College of Radiology summary of the International Commission on Radiological Protection suspected in utero induced deterministic radiation effects.[16]

Abbreviation: MRI, magnetic resonance imaging.

[a]Data on the stochastic effects (ie, radiation-induced cancers, typically childhood leukemias) are inconsistent. For exposure to a newborn child, the lifetime attributable risk of developing cancer is estimated to be 0.4% per 10 mGy dose to the fetus. The potential risks in utero for the second and third trimesters and part of the first trimester may be comparable, but the uncertainties in this estimate are considerable.[16]

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left or right hip displacement during MRI is crucial after 20 weeks' gestation to avoid compressing the inferior vena cava, which could impair venous return and cause discomfort or syncope.[36]

MRI has been reported as useful in evaluating breast cancer[37] and suspected pelvic pathology[44] when ultrasound is inconclusive. MRI without contrast identified nine of 11 known PrBC lesions with close concordance between tumor size on MRI, ultrasound, and pathology.[37] In a prospective study of 34 pregnant patients with abdominal or pelvic pain, MRI matched the final diagnosis in 22 of 23 confirmed cases and helped rule out pathology in 11 others.[44] MRI was also reported to improve characterization of indeterminate ovarian masses[46] and has been proposed as an alternative to bone scintigraphy for suspected bone metastases.[47] Whole-body (WB) diffusion-weighted MRI can be used to diagnose and stage cancer in pregnancy, with high sensitivity and specificity.[45,48]

Computed Tomography

Fetal ionizing radiation doses from computed tomography (CT) imaging were consistently reported to be below the deterministic threshold of 50 mGy. Evidence from observational studies supports the diagnostic utility of CT in urgent, nononcologic clinical scenarios such as trauma, appendicitis, and renal colic, where fetal exposures were generally within accepted safety margins.[23,48] However, the use of CT involving direct fetal exposure, particularly abdominal and pelvic imaging, is associated with higher fetal ionizing radiation doses and is not routinely recommended during pregnancy.

Data on CT for oncologic indications in pregnant patients are limited. No published studies to date have specifically evaluated the use of low-dose CT protocols for cancer staging in pregnancy. Reports of low-dose CT in acute care settings (eg, appendicitis or renal colic) suggest such protocols may be feasible, but its application to oncology remains unstudied.[48] CT imaging of the chest may be considered in selected cases when advanced imaging is critical to management but MRI is contraindicated, and the potential diagnostic benefit outweighs the fetal risk.

PET and PET-CT

A systematic review of four case series and nine case reports totaling 19 patients who underwent positron emission tomography (PET) imaging during pregnancy reported fetal radiation doses averaging 3.97 mGy[49] Most fetal tracer uptake occurred in the brain, myocardium, and urinary system. PET-MRI and techniques such as bladder catheterization were described as methods to further reduce fetal exposure.[45,49]

In a prospective observational study of 63 pregnant patients with cancer, ^{18}F-labeled fluorodeoxyglucose PET-CT altered cancer staging in 60.3% of patients, with a resultant change

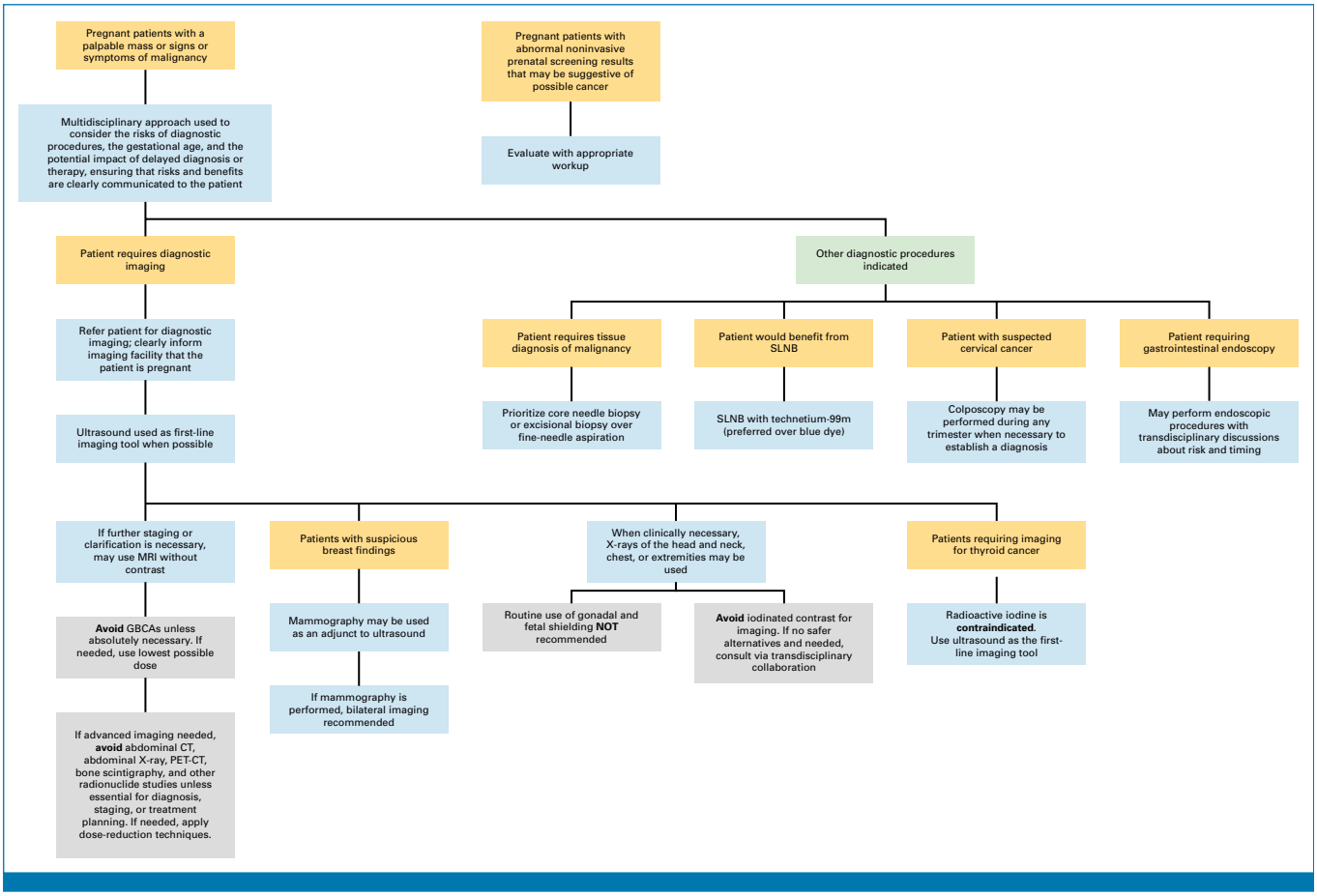

FIG 2. Diagnostic evaluation for pregnant patients with signs or symptoms of cancer. CT, computed tomography; GBCAs, gadolinium-based contrast agents; MRI, magnetic resonance imaging; PET, positron emission tomography; SLNB, sentinel lymph node biopsy.

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in first-line medical treatment, generally due to the identification of lymph node involvement or previously undetected metastases.[50] The majority of patients (50 out of 58 with available pregnancy outcome data) delivered healthy newborns, although there were seven terminations due to cancer severity, and four maternal deaths within 2 years of diagnosis, primarily among patients with metastatic breast cancer. No congenital anomalies or developmental abnormalities were reported in newborns at 2-year follow-up. Furthermore, dose-reduction techniques can further lower fetal exposure.[17]

Use of Contrast Agents in Imaging

Contrast agents may cross the placenta and accumulate in fetal tissues.[51–53] Gadolinium, often used in cancer imaging, is generally avoided during pregnancy because of potential teratogenic risks.[53] While no direct evidence of teratogenicity has been reported in human studies, one large population-based cohort reported rare childhood rheumatologic, inflammatory, or infiltrative skin conditions following in utero exposure to gadolinium.[43] Although there is no significant increase in fetal or neonatal death associated with gadolinium exposure during pregnancy,[52] and no heightened risk of congenital anomalies at any stage of pregnancy,[43] current guidelines discourage the use of gadolinium-based contrast agents (GBCAs) during pregnancy.[54,55] When necessary, GBCAs should be used at the lowest possible dose.[20,36,53] Safer alternatives include gadobenate dimeglumine or gadoterate meglumine.[56]

For iodinated contrast agents administered intravenously, neonatal hypothyroidism is a concern.[48,54,57] Based on existing data and the standard practice of screening all newborns for congenital hypothyroidism through thyroid-stimulating hormone level testing at birth, no additional monitoring is necessary.[54] Oral iodinated contrast remains confined to the GI tract; it is not associated with fetal effects and is considered safe for use during pregnancy.[54] For the diagnosis of thyroid cancer during pregnancy, radioactive iodine is contraindicated; instead, ultrasound is the preferred imaging modality.[20,84,85]

Bone Scintigraphy

Evidence on the safety of bone scintigraphy in pregnancy is limited. According to European Association of Nuclear Medicine (EANM) practice guidelines,[58] a clinical decision

must weigh the benefits against the possible risks of performing bone scintigraphy in a pregnant patient. Bone scintigraphy using an indwelling urinary catheter to avoid retention of radioactive material is recommended only when other imaging modalities, such as MRI, are unavailable or yield inconclusive results.[58-60] MRI is an alternative imaging strategy for suspected bone metastases.[58,60]

Biopsy

Biopsy procedures were widely reported as safe across all trimesters of pregnancy. Most data come from case series and cohort studies involving excisional, core needle, or bone marrow biopsies, and no significant increase in adverse outcomes were observed when compared with nonpregnant cohorts.[56,61,62,86] Biopsies are usually performed under local anesthesia, which is generally considered safe during pregnancy. A tissue or bone marrow biopsy should not be delayed, regardless of the gestational age.[8,56] Nonpelvic lymph node biopsies can be safely performed throughout pregnancy, whereas pelvic lymph node dissection is recommended only up to 22 weeks of gestation due to the growing uterus causing greater technical difficulty.[8]

Sentinel lymph node biopsy (SLNB) has been investigated in pregnant patients with PrBC. A systematic review of 63 studies investigating the use of SLNB for breast cancer in pregnant patients found that the majority of published evidence supports the safety and effectiveness of SLNB in PrBC when clinically indicated.[61] Among the 237 patients with complete data, the overall live birth rate was 95.8%, and the neonatal complication rate was 3.4%. No maternal adverse events or anaphylactic reactions were reported.[61]

In fluorescence imaging, indocyanine green, which has minimal transplacental passage, is considered safe during pregnancy,[80] whereas the use of blue dyes is discouraged due to the small risk of anaphylaxis.[62]

When diagnostic imaging reveals a suspicious mass, an image-guided core or excisional biopsy is the preferred option. Pregnant patients requiring a breast biopsy should be made aware of the minimal risks of developing a milk fistula or experiencing increased bleeding.[23,63] If the mass appears clinically concerning and imaging does not reveal a clear cause, a palpation-guided biopsy without imaging can be performed.[23]

Fine-Needle Aspiration Cytology

In general, fine-needle aspiration (FNA) is not recommended as the initial approach for evaluating a palpable mass, as changes following the procedure can obscure the lesion or complicate imaging interpretation.[23,30] However, if imaging fails to identify the cause of the suspicious mass, FNA may be an option.[23,30]

For certain cancers, particularly thyroid malignancies, FNA remains a gold-standard diagnostic tool.[64] Case reports have demonstrated accurate diagnosis of medullary thyroid carcinoma using FNA combined with immunocytochemistry and biomarker analysis, including calcitonin and thyroid transcription factor-1.[65] In cases where surgical intervention must be delayed, FNA allows for precise diagnosis and treatment planning.[65]

Colposcopy for Cervical Cancer

The reliability of colposcopy during pregnancy, especially for women diagnosed with abnormal cervical cytology, was examined in a multicenter study.[66] Colposcopy had a strong concordance (68%) with histopathological findings and appears to be most effective in the first two trimesters, with its diagnostic accuracy decreasing after 20 weeks due to pregnancy-induced cervical changes, such as hyperemia, metaplasia, and decidual alterations, which can mimic preinvasive disease.[66-68] Biopsies performed during colposcopy are considered safe for the fetus throughout pregnancy and are reliable for diagnostic purposes.[68,69] Endocervical curettage is contraindicated due to its association with miscarriage and preterm delivery.[68]

Upper GI Endoscopy and Colonoscopy

Observational studies and systematic reviews have evaluated the safety of GI endoscopy during pregnancy.[70-72,82,83] A systematic review of lower GI endoscopy procedures, including colonoscopy, reported no etiologic association between the procedures and adverse maternal or fetal outcomes across all trimesters.[72,82] However, included studies were limited by small sample sizes, and few provided control groups or long-term outcome data, limiting the ability to detect rare complications. Upper GI endoscopy is more frequently reported and is generally conducted when clinically indicated.[83]

The use of sedation or anesthesia during endoscopy or colonoscopy poses potential risks to the fetus. Placental blood flow is closely linked to maternal blood pressure and oxygenation, and oversedation leading to maternal hypotension or hypoxia can reduce placental perfusion, causing fetal hypoxia, distress, or even fetal demise.[70,71] According to American College of Obstetricians and Gynecologists (ACOG) guidance, no currently used anesthetic agents have been found to have teratogenic effects when administered in standard doses at any gestational age.[73]

No comparative data exist to assess optimal fetal monitoring practices during endoscopy. ACOG recommends fetal heart rate monitoring based on gestational age, the nature of the procedure, and the facility's resources, as this can assist with maternal positioning and cardiopulmonary management.[73] Recommendations regarding fetal heart rate and uterine contraction monitoring beyond 24 weeks are based on expert consensus rather than empirical evidence. Electronic monitoring of fetal heart rate and uterine contractions is recommended before, during, and after the procedure, ideally overseen by a qualified professional, with obstetric support

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readily available to address any signs of fetal distress or pregnancy-related complications.[71]

Noninvasive Prenatal Screening

A growing number of case reports and small cohort studies have identified abnormal results on noninvasive prenatal screening (NIPS), based on cell-free DNA (cfDNA) analysis, as the initial indication of undiagnosed maternal malignancy. In published series, incidental maternal cancer diagnoses following abnormal or nonreportable NIPS results included melanoma, Hodgkin lymphoma, colorectal cancer, cervical cancer, and breast cancer.[74-77] Findings suggest that NIPS, while not originally designed for cancer detection, can serve as an early sign of cancer by detecting abnormalities in circulating cfDNA arising from maternal cancer cells in the bloodstream, with studies reporting a positive predictive value of up to 75% by combining NIPS with cfDNA.

The IDENTIFY study, a prospective evaluation of pregnant individuals with abnormal cfDNA results, reported cancer diagnoses in 48.6% of participants who underwent follow-up screening using a standardized diagnostic protocol.[78] Among the diagnostic tools assessed, whole-body MRI demonstrated the highest sensitivity (98%) and specificity (88.5%) for malignancy detection. In contrast, serum tumor markers and fecal occult blood tests showed lower diagnostic accuracy. The study did not assess long-term maternal or fetal outcomes associated with early cancer detection.

No studies to date have systematically evaluated whether incidental maternal cancer detection through NIPS alters cancer prognosis or treatment outcomes. Evidence remains limited to case reports and small observational series, and there is currently insufficient data to determine the optimal approach to follow-up or surveillance in these patients. While it has been suggested that patients with abnormal findings should be evaluated with proper history and clinical examination followed by tumor markers and imaging studies as indicated,[64,74-77] cautious interpretation, multidisciplinary evaluation, and informed counseling, rather than reflexive intensive imaging or procedures, are prudent.

Clinical Interpretation for Diagnostic Evaluation

When evaluating pregnant patients with suspected malignancy, clinicians must carefully balance the need for accurate and timely diagnosis and staging against potential embryonic or fetal risks (Table 3) and communicate this clearly to the patient. Before ordering imaging, clinicians should consult a radiologist on the lowest-dose protocols and consider nonionizing alternatives (ultrasound or MRI) whenever they can yield equivalent diagnostic information. All studies should adhere to the ALARA principle, and abdominal shielding is generally discouraged because it offers minimal benefit while possibly increasing scatter and fetal exposure. Imaging and related counseling should be limited to tests that directly influence management. During informed decision making, clinicians should quantify estimated fetal dose of ionizing radiation, explain that deterministic effects are unlikely below 50 mGy, note that stochastic risks such as childhood cancer theoretically increase with any exposure, and reassure patients that doses under 100 mGy are highly unlikely to cause fetal harm. For exposures between 100 and 500 mGy, individualized counseling on the potential for serious fetal harm and long-term cancer risk in the offspring is essential, framing continuation or termination of pregnancy as a personal choice rather than a clinical mandate. Adjunctive diagnostics, serum tumor markers and biopsies, also require nuanced interpretation in pregnancy. Some markers may be physiologically elevated, especially in the third trimester, reducing their specificity. Core needle or excisional biopsy under local anesthesia is preferred for histologic confirmation of malignancy as it preserves tissue architecture and reduces the likelihood of inconclusive results. Sedation should be minimized to avoid fetal hypoxia or preterm labor. Throughout the diagnostic process, clinicians should engage in shared decision making with the patient.

ONCOLOGIC MANAGEMENT

Literature Review and Analysis

A total of 293 studies were included in this review assessing oncologic treatment and fetal outcomes in pregnant patients with cancer. The literature search identified studies that describe treatment with systemic therapy (n = 169),[3-5,8,9,11,56,86-100,101-130,131-160,161-190,191-210,211-230,231-247] RT (n = 30),[1,8,12,120,248-273] and surgery (n = 38).[1,6,8,10,62,83,86,111,137,162,180,274-300] Studies informing supportive care interventions during pregnancy (n = 34)[90,158,301-332] were also included. An additional 37 studies focused specifically on maternal prognosis and survival outcomes across multiple cancer types.[34,86,111,161,180,333-364]

Survival Outcomes in Cancers During Pregnancy

Breast Cancer

Patients diagnosed with PrBC generally have a prognosis comparable to that of nonpregnant patients when treated according to evidence-based guidelines for nonpregnant patients, particularly with timely administration of systemic therapy. Large cohort studies show that overall survival (OS) and disease-free survival (DFS) are not significantly different from matched nonpregnant controls when adjusting for stage at diagnosis and treatment timing, assuming standard oncologic care is provided.[333-337,363] Although PrBC may present more often with advanced-stage or aggressive subtypes, such as human epidermal growth factor receptor 2 (HER2)–positive or triple-negative disease, pregnancy does not appear to worsen prognosis if modern, multidisciplinary

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TABLE 3. Imaging and Other Modalities for Diagnosing Cancer During Pregnancy

Modality	Estimated Fetal Radiation Dose	Uses	1st Trimester Risks (1-12 weeks)	2nd Trimester Risks (13-26 weeks)	3rd Trimester Risks (27-40 weeks)	Precautions and Notes
Imaging						
US	0 mGy	First-line imaging tool. Locoregional staging. Preferred due to the absence of ionizing radiation	No known fetal risk	No known fetal risk	No known fetal risk	B-mode and M-mode preferred. Limit Doppler use due to thermal effects; keep exams under 30 minutes
MRI without contrast	0 mGy	Highly effective for detailed soft-tissue evaluation, especially when US results are inconclusive. Useful for staging and complex conditions requiring deeper tissue imaging DWI and MRI using DTI are useful for assessing burden of disease without contrast	Minimal risk (theoretical concerns about tissue heating and electromagnetic effects)	No known fetal risk	No known fetal risk	1.5T preferred in early pregnancy; reduce SAR. Avoid gadolinium unless essential and use alternatives (gadobenate dimeglumine or gadoterate meglumine)
CT scan head or neck[a]	≤0.01 mGy	Staging	Minimal risk	Minimal risk	Minimal risk	Use when diagnostic benefit outweighs fetal risk; minimal exposure to embryo or fetus
Chest X-ray	≤0.01 mGy	Staging and evaluation of metastases; essential for maternal lung evaluations	Minimal risk	Minimal risk	Minimal risk	Use when clinically necessary; minimal exposure to embryo or fetus
Mammography	<0.03 mGy	Adjunct to US	Minimal risk	Minimal risk	Minimal risk	Breast tissue changes may reduce sensitivity during pregnancy
CT scan chest[a]	0.01-0.66 mGy	Staging and evaluation of metastases	Minimal risk	Minimal risk	Minimal risk	Use when diagnostic benefit outweighs fetal risk; minimal exposure to fetus
Abdominal X-ray	0.1-3.0 mGy	Typically used for noncancer indications	Moderate risk (IUGR or organ malformations at higher doses)	Moderate risk (IUGR possible at high doses, >50 mGy)	Lower risk (still use caution due to ionizing radiation exposure)	Use only for essential diagnostic purposes
T-99m bone scintigraphy	4-5 mGy	Staging and evaluation of bone metastases	High risk (ionizing radiation exposure 5-10 mGy, radioactive tracers cross placenta and can interfere with organogenesis)	Moderate risk (potential IUGR, avoid)	Moderate risk (potential IUGR, use only if essential)	Hydration and bladder catheterization to reduce fetal exposure if scan necessary for management during pregnancy. Seek alternatives when possible
CT scan abdominal/pelvic[a]	1.3-35 mGy 10-50 mGy	Detailed imaging for staging but used sparingly due to potential ionizing radiation risks	High risk (miscarriage, teratogenic effects, increased childhood cancer risk)	High risk (IUGR and developmental issues)	High risk (functional impairments possible)	Risk of IUGR and fetal effects increases with dose. Use sparingly and only if essential for maternal diagnosis
PET-CT	10-50 mGy	Staging	High risk (radiation risk from radiotracers crossing placenta, potential teratogenic effects)	Moderate risk (potential developmental or functional effects)	Moderate risk (potential for functional impairments, although risk reduced compared with earlier trimesters)	Avoid during pregnancy unless no alternatives exist; encourage hydration and catheterization to reduce exposure. Low-dose protocols recommended

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TABLE 3. Imaging and Other Modalities for Diagnosing Cancer During Pregnancy (continued)

Modality	Estimated Fetal Radiation Dose	Uses	1st Trimester Risks (1-12 weeks)	2nd Trimester Risks (13-26 weeks)	3rd Trimester Risks (27-40 weeks)	Precautions and Notes
Blood tests						
Serum tumor markers	NA	May be useful in the diagnosis, follow-up, and management of patients with cancer, especially when diagnostic imaging is inconclusive	No known fetal risk	No known fetal risk	No known fetal risk	Some tumor markers may lack sensitivity and specificity during pregnancy, due to physiologic variations in serum levels *Markers reliable in pregnancy*: CEA and CA 19-9, although can increase in third trimester HE-4 LDH AMH *Can be elevated during normal pregnancy*: MSAFP CA 15.3 *Not useful for diagnosing adnexal or mediastinal masses in pregnancy*: CA125 AFP hCG
Biopsy, FNA, and surgical staging						
Biopsy	NA	The benefits of open biopsies for diagnostic purposes often outweigh the risks and should not be withheld	Minimal risk (avoid deep sedation or general anesthesia)	Minimal risk (avoid prolonged procedures)	Minimal risk (consider risks of preterm labor due to procedural stress)	Local anesthesia is safe. When feasible, a core needle or excisional biopsy is preferred over cytology from a fine-needle aspirate, to preserve tissue architecture and to avoid delays in diagnosis. Pregnancy itself may induce changes in tissues that could mimic malignancy, and pathologists should be informed of the pregnancy to reduce misdiagnosis
SLNB	≤0.014 mGy	Lymph node involvement and staging	High risk (from ionizing radiation exposure)	Moderate risk	Moderate risk	Radiocolloid is safer than blue dye. Allergic reactions and placental transfer possible with dye use
FNAc	NA	Useful for cytological assessment but may require additional tests for conclusive results	Minimal risk	Minimal risk	Minimal risk	Core biopsy is preferred except for thyroid cancer suspicion. Local anesthesia is safe. Can be inconclusive, requiring further diagnostic steps. Postaspiration changes may obscure lesion visualization or negatively impact image interpretation
Colposcopy	NA	Good concordance with histopathologic findings, particularly when performed in trimester 1-2. Effectiveness declines as pregnancy progresses	Minimal risk	Minimal risk	Minimal risk	Avoid endocervical curettage due to preterm labor risk. Colposcopic biopsy is acceptable if clinically required

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TABLE 3. Imaging and Other Modalities for Diagnosing Cancer During Pregnancy (continued)

Modality	Estimated Fetal Radiation Dose	Uses	1st Trimester Risks (1-12 weeks)	2nd Trimester Risks (13-26 weeks)	3rd Trimester Risks (27-40 weeks)	Precautions and Notes
Upper GI endoscopy or colonoscopy	NA	Useful to visualize and biopsy abnormalities in the upper GI tract, colon, or rectum	Minimal risk	Minimal risk	Moderate risk	Use minimal sedation and monitor maternal oxygenation to avoid fetal hypoxia. Avoid deep sedation or agents that cross the placenta in significant amounts. Short-acting sedatives are typically considered safe in small doses. Use pregnancy-safe bowel preparation agents, avoid saline laxatives and magnesium citrate due to risks of dehydration and electrolyte imbalance. PEG-based solutions preferred. Minimize dehydration, as it may lead to uterine contractions

Abbreviations: AFP, alpha-fetoprotein; AMH, anti-Müllerian hormone; CA, cancer antigen; CEA, carcinoembryonic antigen; CT, computed tomography; DTI, diffusion tensor imaging; DWI, diffusion-weighted imaging; FNA, fine-needle aspiration; FNAc, fine-needle aspiration cytology; hCG, human chorionic gonadotropin; HE-4, human epididymis protein 4; IUGR, intrauterine growth restriction; LDH, lactate dehydrogenase; MRI, magnetic resonance imaging; MSAFP, maternal serum alpha-fetoprotein; NA, not applicable; PEG, polyethylene glycol; PET, positron emission tomography; SAR, specific absorption rate; SGA, small for gestational age; SLNB, sentinel lymph node biopsy; T99m; technetium-99m; US, ultrasound.

[a]Avoid IV iodinated contrast when possible. If required, ensure discussion of possible neonatal hypothyroidism.

management is maintained.[34,335,339] Notably, however, one meta-analysis and one additional cohort study reported poorer survival and higher cancer mortality in PrBC compared with nonpregnancy-associated breast cancer, highlighting the importance of timely diagnosis, close clinical monitoring, and individualized treatment planning.[340,341]

Gynecologic Cancer

For cervical cancer, multiple studies reported no significant survival difference between pregnant and nonpregnant patients, with 5-year OS rates over 70%.[342] Results from a meta-analysis show the 5-year OS of patients with cervical cancer in pregnancy was similar to that of nonpregnant patients with cervical cancer.[343] However, some studies have suggested that outcomes may depend on the timing of the diagnosis. A meta-analysis found poorer prognosis for cases diagnosed postpartum,[343] another cohort study reported higher mortality for cases diagnosed during pregnancy,[344] and another found prognosis did not differ between patients diagnosed before and after delivery.[345] Data on other gynecologic malignancies, including ovarian, endometrial, and vulvar cancers, remain limited. In pregnancy, diagnosis is often incidental, particularly for ovarian cancer.[286] Reported outcomes appear more strongly associated with tumor type and stage than with pregnancy status.[180,346,347,364]

GI Cancer

The International Network of Cancer, Infertility and Pregnancy (INCIP) registry, which includes 131 cases of maternal deaths, showed a higher percentage of women diagnosed with gastroesophageal cancer compared with the control group of women with a cancer diagnosis during pregnancy who did not die within 1 year after delivery.[363] In colorectal cancer, pregnancy was associated with later-stage diagnosis, attributed to symptom overlap with pregnancy, but survival did not differ significantly after adjustment for disease extent.[348,349] Similar patterns were reported for gastric cancer, with no clear evidence of worsened prognosis.[348,350]

Other Solid Tumors

Evidence on lung cancer during pregnancy remains limited. While individual case reports and registry data describe poor outcomes,[351,363] larger registry studies found no statistically significant increase in mortality compared with nonpregnant controls.[340] Pregnancy was not associated with worsened prognosis in sarcomas.[340] For melanoma, diagnosis during pregnancy does not appear to worsen prognosis when compared with nonpregnant individuals, with disease stage appearing to be the strongest determinant of prognosis.[86,352,353]

Hematologic Cancer

Survival outcomes for hematologic malignancies, including lymphoma and leukemia, did not differ significantly between pregnant and nonpregnant patients across included studies.[111,161,354-357] Findings from cohort studies show that prognosis in Hodgkin lymphoma and non-Hodgkin lymphoma is largely dependent on histologic subtype and treatment timeliness.[357] Similarly, prognosis for acute leukemia during pregnancy is influenced by the rapid initiation of induction therapy, sometimes necessitating pregnancy termination. Studies describe significant rates of maternal morbidity and mortality compared with nonpregnant women with acute leukemia.[357]

Neurologic and Endocrine Cancers

No survival differences were reported in gliomas,[358] thyroid cancer,[359,360] or other endocrine tumors.[340]

Impact of Timing of Treatment Initiation on Prognosis

Delays in cancer treatment are a consistently poor prognostic factor in all people with cancer. A meta-analysis across multiple tumor types showed that a 4-week delay in cancer treatment increases mortality due to higher recurrence and metastasis risks.[361] A retrospective review of 5,137 patients with invasive primary breast cancer found that delaying neoadjuvant chemotherapy beyond 61 days after diagnosis was significantly associated with increased mortality (hazard ratio, 1.28 [95% CI, 1.06 to 1.54]).[362] Among patients with HER2-positive breast cancer, earlier recurrence (P = .008) was reported for cancers diagnosed during pregnancy compared with nonpregnant controls.[335] This difference in survival may be partly explained by the absence of anti-HER2 therapy in the pregnancy group, as deferring targeted treatment could negatively impact DFS, despite similar OS outcomes.[335] Other data suggest that differences in survival are attenuated or eliminated after controlling for confounders such as tumor stage and timing of treatment initiation.[334,336]

Overall, the cumulative evidence indicates that the prognosis for pregnant patients with cancer is primarily driven by tumor stage and biology, and prompt initiation of evidence-based treatment, rather than pregnancy status. When standard-of-care treatment can be initiated without delay, outcomes in pregnant patients are comparable to those in nonpregnant populations.

Systemic Therapy

This section is organized by therapeutic class (Table 4). Although the evidence base for systemic therapy in pregnant patients is largely composed of case reports and small observational studies, the quality was upgraded from low to moderate when findings were consistent across multiple sources, when serious or clinically meaningful harms were repeatedly observed, and when the direction and magnitude of effects were supported by established pharmacologic or biologic understanding. In such cases, the consistency of findings across studies, the alignment with known biological mechanisms, and the potential impact on patient or fetal outcomes supported greater confidence in the findings despite limitations in study design. The interpretation of the

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TABLE 4. Systemic Cancer Treatment During Pregnancy

Therapy Type	Agent(s)	First Trimester Use	Second Trimester Use	Third Trimester Use	Safety Concern
Alkylators	Cyclophosphamide ifosfamide Dacarbazine	High risk	Acceptable with monitoring	Acceptable with monitoring	High rates of miscarriage, congenital malformations, and embryonic and fetal toxicity with first-trimester exposure. Potential use in T2 and T3 with caution. Breast cancer dosing is generally safe in T2, T3. Doses for lymphoma have been used in T2, T3 without fetal malformations. However, risk of preterm birth when used in T2, T3 remains
Antimetabolites	Methotrexate 5-FU Capecitabine Gemcitabine	High risk	MTX: High risk 5-FU, capecitabine, gemcitabine: Limited safety data—Caution advised	MTX: High risk 5-FU, capecitabine, gemcitabine: Limited safety data—Caution advised	Methotrexate is highly teratogenic and an abortifacient and should not be used in pregnancy. 5-FU carries risks of spontaneous abortion and malformations if used in the first trimester. Potential use of 5-FU, capecitabine, and gemcitabine in T2 and T3 with caution; however, gemcitabine and capecitabine linked to IUGR. *DPYD* testing in pregnant patients who will receive 5FU or capecitabine is recommended
Platinum	Cisplatin Carboplatin Oxaliplatin	High risk	Acceptable with monitoring	Acceptable with monitoring	Platinum agents, with a preference for carboplatin, have been used safely in T2, T3, but potential risks for ototoxicity and hypothyroidism in fetuses, and a smaller fetus size for gestational age. Recommend postnatal auditory BAER testing over OAE screening at birth
Anthracyclines	Doxorubicin Daunorubicin Idarubicin Epirubicin Bleomycin	High risk	Idarubicin: High risk Other anthracyclines: Generally considered safe	Idarubicin: High risk Other anthracyclines: Generally considered safe	Idarubicin contraindicated in all trimesters. Use of other anthracyclines during second and third trimester of pregnancy has resulted in fewer fetal complications than the first trimester, although there is a risk of preterm birth and low birth weight; cardiac function should be monitored
Topoisomerase inhibitors	Irinotecan Etoposide	High risk	Limited safety data—Caution advised	Limited safety data—Caution advised	Topoisomerase inhibitors have been used safely in T2 and T3, however, etoposide is associated with IUGR and cytopenias. Irinotecan may be less teratogenic. Preterm birth and fetal or neonatal myelosuppression possible
Vinca alkaloids	Vincristine Vinblastine Vinorelbine	High risk	Acceptable with monitoring	Acceptable with monitoring	First trimester associated with spontaneous abortion and rare malformations. Later exposure generally considered safe; rare reports of fetal cytopenias or anomalies
Taxanes	Paclitaxel Docetaxel	High risk	Acceptable with monitoring	Acceptable with monitoring	Favorable toxicity profile with use in T2, T3 but potential risks of preterm birth and low birth weight, and maternal toxicity
Hormonal therapy	Tamoxifen Aromatase inhibitors GnRH agonists	High risk	High risk	High risk	Tamoxifen associated with fetal anomalies including genital and craniofacial defects. AIs and GnRHa contraindicated based on preclinical data and hormonal disruption For hormone-sensitive cancers, consider alternative treatments or delay therapy until delivery
HER2-targeted therapy	HER2-targeted TKIs Lapatinib Neratinib	High risk	High risk	High risk	Lapatinib and neratinib are contraindicated. Lapatinib is associated with IUGR and neratinib has shown embryo-fetal toxicity, including fetal death and structural abnormalities in preclinical studies
	HER2-targeted mAbs Trastuzumab Pertuzumab	Limited safety data—Caution advised	High risk	High risk	Trastuzumab in T2/T3 associated with oligohydramnios, fetal renal dysfunction, and congenital malformations. Pertuzumab has limited safety data and higher placental transfer. Exclusive exposure during first trimester of pregnancy appears not to be associated with abnormalities

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TABLE 4. Systemic Cancer Treatment During Pregnancy (continued)

Therapy Type	Agent(s)	First Trimester Use	Second Trimester Use	Third Trimester Use	Safety Concern
VEGF/VEGFR-targeted therapy	VEGF mAbs Bevacizumab Ramucirumab Aflibercept	High risk	High risk	High risk	Contraindicated throughout pregnancy due to disruption of placental vasculature, fetal resorption, and growth restriction seen in animal studies. No reassuring human data are available
EGFR-targeted therapy	EGFR mAbs Cetuximab	Limited safety data—Caution advised	Limited safety data—Caution advised	Limited safety data—Caution advised	Safety unclear due to limited number of cases of use during pregnancy and need for more safety data
	EGFR-targeted TKIs Erlotinib Gefitinib Afatinib Osimertinib	High risk	Limited safety data—Caution advised	Limited safety data—Caution advised	Limited number of cases during pregnancy revealed no pattern of congenital malformations. More safety data is needed
ALK-targeted therapy	ALK-targeted TKIs Crizotinib Alectinib	High risk	Limited safety data—Caution advised	Limited safety data—Caution advised	Limited case reports with no major anomalies, but preclinical studies show fetal harm. Use only if no safer alternatives are available
ABL kinase-targeted therapy	ABL-targeted TKIs Imatinib Nilotinib Dasatinib	High risk	Dasatinib: High risk Others: Limited safety data—Caution advised	Dasatinib: High risk Others: Limited safety data—Caution advised	Congenital abnormalities and spontaneous abortions have occurred after the administration in early pregnancy. Preclinical and case data suggest risk of FGR, malformations with dasatinib. Potential use of imatinib, nilotinib in T2, T3 with caution
CD20 targeted therapy	CD20 mAbs Rituximab	Limited safety data—Caution advised	Acceptable with monitoring	Acceptable with monitoring	Not teratogenic but causes transient neonatal cytopenias. Postnatal immune follow-up recommended
MEK and RAF targeted therapy	MEK-targeted TKIs Trametinib	High risk	High risk	High risk	Embryotoxic and teratogenic in animal models. No reassuring human data
	BRAF-targeted TKIs Vemurafenib Dabrafenib	High risk	Limited safety data—Caution advised	Limited safety data—Caution advised	Limited human data suggest risk of prematurity and IUGR. Vemurafenib appears better tolerated than dabrafenib. Caution in patients with sulfa allergies or use after or with immunotherapy
Antibody-drug conjugates	Trastuzumab emtansine	High risk	High risk	High risk	Limited evidence of trastuzumab emtansine use during pregnancy suggests potential signal for increased risk of cardiovascular malformations
	Other ADCs such as trastuzumab deruxtecan, sacituzumab govitecan, mirvetuximab soravtansine, tisotumab vedotin, enfortumab vedotin, datopotamab deruxtecan, brentuximab vedotin	High risk	Limited safety data—Caution advised	Limited safety data—Caution advised	Limited evidence of brentuximab vedotin use during pregnancy, caution advised
Immunotherapy	ICIs Pembrolizumab Nivolumab ipilimumab	Limited safety data—Caution advised	High risk—Use only if essential	High risk—Use only if essential	Risks include IUGR, stillbirth, premature delivery, and infant mortality, especially when used throughout the third trimester in animal studies; safety unclear due to limited human data and insufficient long-term data. Combination ICI regimens may carry higher risks. Use only in life-threatening maternal situations

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TABLE 4. Systemic Cancer Treatment During Pregnancy (continued)

Therapy Type	Agent(s)	First Trimester Use	Second Trimester Use	Third Trimester Use	Safety Concern
Cellular therapy	CAR T-cell therapy Tisagenlecleucel axicabtagene ciloleucel	Unknown risk	Unknown risk	Unknown risk	CAR T-cell therapy is contraindicated during pregnancy. No human or animal pregnancy data. Theoretical risk of fetal toxicity from transplacental migration of modified T-cells
	Hematopoietic cell transplantation	High risk	High risk	High risk	HCT is contraindicated during pregnancy
Interferon	Interferon-alpha	Low risk	Low risk	Low risk	Limited placental transfer and safe in any trimester
PARP inhibitors	Olaparib Niraparib Rucaparib	High risk	High risk	High risk	Based on mechanism of action and animal studies, PARP inhibitors can cause teratogenicity, embryo-fetal toxicity, and/or death

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Abbreviations: ABL, Abelson tyrosine kinase; ADC, antibody-drug conjugate; AIs, aromatase inhibitors; ALK, anaplastic lymphoma kinase; BAER, brainstem auditory evoked response; BRAF, v-Raf murine sarcoma viral oncogene homolog B1; CAR-T, chimeric antigen receptor T-cell therapy; CD20, cluster of differentiation 20; EGFR, epidermal growth factor receptor; GnRHa, gonadotropin-releasing hormone agonists; HCT, hematopoietic cell transplantation; HER2, human epidermal growth factor receptor 2; ICI, immune checkpoint inhibitor; IUGR, intrauterine growth restriction; mAbs, monoclonal antibodies; MEK, mitogen-activated protein kinase; MTX, methotrexate; OAE, otoacoustic emissions; PARP, poly (ADP-ribose) polymerase; T1, T2, T3, first, second, and third trimesters; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor; 5-FU, 5-fluorouracil.

available data should consider the inherent heterogeneity in study designs, cancer types, and timing of treatment.

Chemotherapy

Overall safety and timing. Existing data and guidelines suggest that many conventional chemotherapeutic agents are generally safe to use after 12-14 weeks of gestation, but chemotherapy is largely contraindicated during the first trimester due to the high risk of teratogenicity and embryotoxicity.[3,8,11,56,87-93] In a large cohort of 755 pregnant patients, major congenital anomalies occurred in 21.7% of pregnancies when chemotherapy was initiated before 12 weeks of gestation, versus 3% when chemotherapy began after 12 weeks, a rate comparable to that of the general population.[11] Similarly, a prospective cohort of 225 pregnant patients showed an increased risk of spontaneous preterm birth when chemotherapy was administered before 18 weeks, minor malformations when started before 17 weeks, and FGR when initiated before 15 weeks.[94]

In general, chemotherapy protocols for pregnant patients should follow the guidelines used for nonpregnant patients. Pregnancy-related physiological changes (increased plasma volume and altered drug clearance) can affect pharmacokinetics, but existing data support the use of standard dosing based on actual weight during pregnancy.[6-10] After 34 weeks, therapy is usually paused to allow for maternal and fetal hematologic recovery before delivery, although some regimens can be extended closer to term.[8,236] Close collaboration between oncology and maternal fetal medicine (MFM) is required.

When feasible, visibly pregnant patients receiving systemic therapy should be offered the option of a private or more discreet infusion setting, as receiving treatment in shared spaces may lead to uncomfortable interactions or reactions from others. This consideration can significantly impact the patient's emotional well-being and overall treatment experience.

Alkylating agents. Alkylating agents, such as cyclophosphamide, ifosfamide, and dacarbazine, have been used safely in standard regimens (eg, cyclophosphamide, doxorubicin, vincristine, and prednisolone; and doxorubicin, bleomycin, vinblastine, and dacarbazine [ABVD]), with the most robust safety data available for cyclophosphamide. When administered after the first trimester, cyclophosphamide has not been associated with an increased risk of major congenital anomalies,[95-97] and long-term follow-up indicates generally reassuring neurodevelopmental outcomes.[98,99] However, several studies have reported a higher incidence of FGR, low birth weight, and preterm delivery, which may be attributable to both drug effects and underlying maternal conditions.[100-102] In contrast, first-trimester exposure to cyclophosphamide carries a significant teratogenic risk, with reports of craniofacial, limb, and skeletal anomalies.[103,104]

Data on ifosfamide and dacarbazine in pregnancy are limited but reassuring in later trimesters. Ifosfamide has primarily been used for sarcoma, with case reports describing healthy infants following exposure in the third trimester with no observed malformations.[105,106] Dacarbazine, used mainly in the ABVD regimen for Hodgkin lymphoma, has been reported in multiple cohorts and registries, with no consistent pattern of adverse fetal effects when exposure occurs after organogenesis.[107-109] Although earlier delivery and lower birth weights have occasionally been observed, long-term developmental outcomes are generally favorable.[110]

High-dose alkylators, such as busulfan, ifosfamide, and melphalan, and some combination regimens, such as bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisolone (BEACOPP), remain contraindicated or strongly discouraged at any time during pregnancy because of documented embryotoxicity.[5,56,111]

Antimetabolites. Methotrexate is strongly contraindicated in pregnancy, especially during the first trimester, owing to its well-established teratogenic effects. It acts as a folate antagonist and disrupts DNA synthesis and cell division, leading to a high risk of spontaneous abortion, fetal demise, and congenital anomalies, including neural tube defects, craniofacial malformations, limb abnormalities, and growth restriction.[112,113] Most available data come from its use in ectopic pregnancy or rheumatologic diseases; however, these findings are considered generalizable to oncologic contexts. Case reports and systematic reviews have described adverse fetal outcomes, even at low doses and with early, limited exposure.[114-116]

5-fluorouracil (5-FU), an antimetabolite widely used in GI and breast cancers, is contraindicated during the first trimester because it is associated with spontaneous abortion and major congenital anomalies, particularly craniofacial, cardiac, and limb defects.[117,118] However, when administered during the second and third trimesters, 5-FU has been used with caution with generally acceptable fetal outcomes, especially as part of combination regimens such as 5-FU, epirubicin, and cyclophosphamide in breast cancer or with oxaliplatin for colorectal cancers.[102]

Capecitabine, an oral prodrug of 5-FU, is less commonly used during pregnancy because of limited safety data. Although some case reports suggest tolerability in the second and third trimesters, there is insufficient evidence to confirm its safety, and it is generally avoided because of its unpredictable pharmacokinetics and longer exposure profile.[99,235]

Recent studies and reviews show that preemptive *DPYD* genotyping identifies high-risk patients for severe fluoropyrimidine toxicity, enabling upfront dose individualization that substantially reduces hospitalizations and treatment interruptions.[237-240] Dose individualization based on *DPYD* status has been shown to markedly reduce grade 3 to 4 adverse events and unplanned hospitalizations, thereby minimizing maternal morbidity and potential fetal harm from complications such as dehydration or infection.[239,241] Implementation studies, from opt-out testing programs to

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in-house assays, demonstrate that routine *DPYD* testing is feasible across diverse clinical settings and may confer a survival advantage for variant carriers when therapy is appropriately adjusted.[239,240,242,243]

Gemcitabine, another pyrimidine analog, has also been used with caution in the later stages of pregnancy. Although major malformations are rare when exposure occurs after the first trimester, studies suggest a possible association with intrauterine growth restriction (IUGR), especially when used in combination regimens during the second or third trimester.[99,119] Preterm birth and low birth weight have been observed, although it remains unclear whether this is due to the drug itself or underlying maternal disease.

Platinum agents. Platinum agents, particularly cisplatin and carboplatin, appear safe in the second and third trimesters, although risks of low birth weight and ototoxicity have been reported. Systematic reviews and meta-analyses in ovarian and cervical cancer populations have shown that cisplatin and carboplatin are effective and not associated with an increased risk of congenital anomalies when administered after the first trimester, although a modest increase in preterm birth and lower birth weight have been observed.[123-125] Similarly, a large international cohort study found no excess in major birth defects with platinum-based regimens initiated after organogenesis.[102] Case reports involving cisplatin- or carboplatin-based regimens in a range of cancers, including ovarian, neuroendocrine, rectal, colon, and small cell lung cancers, have demonstrated successful maternal and neonatal outcomes.[126-131] Ototoxicity is a recognized risk with platinum agents, cisplatin more so than carboplatin, with documented cases of neonatal hearing loss following in utero exposure,[132,133] indicating a potential need for routine auditory follow-up in exposed infants. Regarding oxaliplatin, multiple case reports involving its use in colorectal cancer during pregnancy described healthy neonatal outcomes without evident congenital abnormalities,[126,127,134,135] although safety data remain limited compared with cisplatin and carboplatin.

Anthracyclines. Anthracyclines, such as doxorubicin, epirubicin, and daunorubicin, are among the most commonly used chemotherapeutic agents during pregnancy, particularly in the treatment of hematologic malignancies. Doxorubicin and epirubicin have low transplacental transfer and are not associated with increased risk of malformation when administered after the first trimester.[121,137] Although epirubicin was previously considered less cardiotoxic, rare cases of transient ventricular hypokinesia and fatal fetal cardiotoxicity have been documented.[138,139] Daunorubicin also has low placental transfer but, when administered during the first trimester, is associated with increased fetal risks, including fetal death and congenital malformations.[140] Idarubicin carries the highest concern due to lipophilicity and fetal accumulation, leading to greater fetal exposure and a higher rate of anomalies and fetal death.[136,140,141] Reports describe limb defects, cardiac dilation, and cardiomyopathy following in utero exposure, even when administered in the second trimester.[142-146]

Topoisomerase inhibitors. Data on the use of topoisomerase inhibitors, particularly etoposide and irinotecan, during pregnancy remain limited to case reports and small series, making risk evaluation difficult. Etoposide, used more often in hematologic malignancies, has been administered in the second and third trimesters with generally acceptable neonatal outcomes, although cases of neonatal myelosuppression have been reported.[4,8,235] First-trimester use is associated with a higher risk of congenital malformations and is generally avoided. Irinotecan has been reported in several cases of colorectal cancer diagnosed during pregnancy, particularly in the second or third trimester, often as part of folinic acid, 5-FU, and irinotecan regimen, or folinic acid, 5-FU, oxaliplatin, and irinotecan regimen.[147-150] In these reports, fetuses exposed to irinotecan did not exhibit major congenital anomalies, although premature birth and low birth weight were occasionally observed. One neonate exposed to irinotecan and 5-FU had postnatal neutropenia and jaundice.[148]

Vinca alkaloids. Vinca alkaloids, including vincristine, vinblastine, and vinorelbine, are used safely after organogenesis, especially in lymphoma protocols. First-trimester exposure is generally avoided owing to the risks of teratogenicity and spontaneous abortion.[137] Second- and third-trimester use appears to have a lower risk profile, although isolated fetal complications such as atrial septal defect, bilateral radius and fifth digit absence, hydrocephalus, renal and cardiac abnormalities, and intrauterine death have been reported.[111] Vinblastine, a key component of the ABVD regimen, has been frequently used in the second and third trimesters with no consistent pattern of malformations observed.[111,151,152] Several clinical reviews and cohort studies support its relative safety in late pregnancy.[153,154] Vinorelbine has been administered in both adjuvant and metastatic settings, with five of six reported infants born healthy and without congenital anomalies at follow-up ranging from 6 to 35 months.[244] Although these findings are reassuring, the number of exposed pregnancies remains small.

Taxanes. An expanding body of evidence suggests that taxanes, principally paclitaxel and docetaxel, appear safe during the second and third trimesters, with no significant increase in congenital anomalies or developmental delays. A large international cohort study of pregnant patients with breast cancer treated with taxanes reported no increase in congenital anomalies, neonatal complications, or developmental delays, reinforcing their safety in the second and third trimesters.[155] These findings are consistent with earlier systematic reviews, which concluded that taxanes, when used after organogenesis, were not associated with an increased teratogenic risk.[156,157] A multicenter retrospective study also found no increased rates of preterm delivery, low birth weight, or neonatal intensive care admissions in taxane-exposed pregnancies.[158] Meconium studies have detected intact paclitaxel and its metabolites in neonates following in utero exposure, confirming placental passage at a low level[159]; however, follow-up data showed no adverse short-term developmental effects among these exposed infants.[160]

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Their use is also supported in combination regimens for gynecologic and hematologic cancers. A systematic review of immunochemotherapy in hematologic cancers, which included taxanes, found acceptable fetal outcomes, although there was a lack of formal clinical trial inclusion for pregnant patients.[161] Similarly, a case series and literature review of paclitaxel plus platinum agents in cervical cancer and gynecologic malignancies showed positive maternal responses without identifiable patterns of fetal harm.[124,162]

Hormonal Therapy

Tamoxifen exposure during pregnancy has been associated with a higher incidence of fetal abnormalities than that in the general population, although the evidence is largely based on case reports and retrospective data. Systematic reviews of published cases report major anomalies in approximately 12%-20% of exposed pregnancies, including genital tract anomalies, craniofacial defects, and Goldenhar syndrome.[163,164] However, most infants were born without major anomalies, and many exposures occurred only in the first trimester or stopped shortly after pregnancy was discovered. An additional documented healthy live birth following tamoxifen exposure during early pregnancy has also been reported.[165] Data on long-term outcomes are scarce.

Aromatase inhibitors (AIs), such as letrozole and anastrozole, are generally contraindicated during pregnancy because of the evidence of teratogenicity in animal models, including skeletal malformations and embryotoxicity.[166] Human data are limited and are primarily derived from patients in whom AI was used for ovulation induction. Some studies have reported favorable pregnancy outcomes without a significant increase in congenital anomalies, although isolated cases of malformations, such as disorders of sex development, have been reported.[167] The evidence remains inconclusive and caution is advised when considering AI use in patients who are or may become pregnant.

Gonadotropin-releasing hormone agonists (GnRHa), including leuprolide, are contraindicated during pregnancy because evidence from animal studies indicates potential fetal harm, such as major malformations and increased fetal mortality. Human data are sparse; however, some reports on inadvertent exposure during early pregnancy have not demonstrated a consistent pattern of malformations.[168-171] Nevertheless, owing to the lack of robust data and potential biological plausibility of harm, tamoxifen, GnRHa, and AIs should be avoided during pregnancy, and any unintentional exposure should prompt close fetal monitoring and multidisciplinary management.

Targeted Therapies

The use of targeted therapies during pregnancy remains limited due to sparse clinical data and known or suspected fetal risks. Antiangiogenic agents, such as tyrosine kinase inhibitors (TKIs) during organogenesis and monoclonal antibodies targeting vascular endothelial growth factor (VEGF) throughout pregnancy, have shown teratogenic effects in animal models and insufficient safety data in humans.[5]

HER2-targeted therapy. Lapatinib exposure during pregnancy has been associated with adverse fetal outcomes, most notably IUGR.[172] Although data from clinical trials are limited, retrospective analyses, such as the NeoALTTO and ALTTO trials, included cases of accidental lapatinib exposure early in pregnancy; these exposures were generally brief and not linked to major malformations, although the sample size was small and follow-up limited.[173] In contrast, evidence for neratinib exposure during pregnancy is restricted to preclinical animal studies, which have shown embryo-fetal toxicity, including fetal death and structural abnormalities, leading to its classification as a contraindication during pregnancy.[174,365] Given the potential for fetal harm, both agents should be avoided during pregnancy, and effective contraception should be advised during treatment and for a period after discontinuation.

Trastuzumab has been associated with oligohydramnios and fetal renal dysfunction, especially when administered in the second or third trimester.[172,173,175-179] If oligohydramnios is present in second trimester, there is a risk of pulmonary hypoplasia, which can result in neonatal demise. Accidental first-trimester exposure may be less risky, but established practice still advises against trastuzumab in pregnant patients.[172,175,176] Pertuzumab exposure during pregnancy is associated with significant fetal risks, particularly oligohydramnios, renal abnormalities, and neonatal kidney failure. A large pharmacovigilance study found increased odds of these outcomes following anti-HER2 exposure, including pertuzumab.[172] A case report also described fetal renal agenesis and oligohydramnios following first and second trimester pertuzumab and trastuzumab use, leading to pregnancy termination.[178]

VEGF and VEGFR-targeted therapy. VEGF inhibitors, such as bevacizumab and aflibercept, are utilized in oncology and ophthalmology but raise concerns regarding fetal safety when administered during pregnancy. Preclinical studies have demonstrated that systemic administration of these agents can lead to FGR, malformations, and embryotoxicity due to their antiangiogenic effects.[180,181] Human data are limited and primarily consist of case reports and pharmacovigilance analyses. While some case reports have described healthy births following bevacizumab use during pregnancy,[182] others have reported adverse outcomes, including spontaneous abortion following intraocular injection.[183,184] This theoretical risk is supported by VEGF's known role in trophoblast proliferation and placental vascular development, making any disruption potentially harmful to fetal growth and viability.[185]

EGFR-targeted therapy. The use of cetuximab during pregnancy has not been well studied in humans, and no large case series are available. However, animal studies have shown increased rates of fetal loss and developmental

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abnormalities following cetuximab exposure, likely due to interference with the epidermal growth factor receptor (EGFR) pathways essential to fetal organogenesis.[118,366] Same recommendations would be made for panitumumab.

Systematic reviews and case reports[186-189] described the use of EGFR TKIs erlotinib and gefitinib during the second and third trimesters in pregnant patients with metastatic non–small cell lung cancer (NSCLC) and an EGFR mutation. In these patients, treatment was associated with stable maternal disease, delivery of healthy term infants without structural abnormalities, and normal long-term neurodevelopment (up to 5-6 years). Pharmacokinetic analyses indicated limited placental transfer and no evidence of fetal toxicity,[186] supporting the cautious and individualized use of EGFR TKIs in pregnancy under multidisciplinary supervision.

Two case reports described exposure to afatinib and osimertinib during pregnancy.[187,190] A single case involving a very brief exposure to afatinib during the early first trimester (<6 weeks' gestation) is notable in that it did not result in any apparent congenital malformations or immediate adverse neonatal effects.[190] Another pregnant patient with lung cancer was treated with osimertinib and trastuzumab beginning at 27 weeks' gestation, resulting in premature labor and delivery at 30 weeks; the newborn experienced transient renal failure and respiratory distress, both of which resolved and the child showed normal development at 8-month follow-up.[187] However, due to the scarcity of data, the use of afatinib and osimertinib during pregnancy should be approached with caution, and decisions should be made on a case-by-case basis, weighing maternal benefits against potential fetal risks.

ALK-targeted therapy. Five published case reports described the use of anaplastic lymphoma kinase (ALK) TKIs during pregnancy in patients with ALK-rearranged NSCLC, including alectinib and crizotinib. A patient who became pregnant during treatment with alectinib and continued treatment throughout pregnancy delivered a healthy term neonate with no reported congenital anomalies or immediate complications.[191] Similar results have been reported where alectinib did not seem to affect embryofetal or early childhood development.[187,192] In two other patients, crizotinib was administered during pregnancy. Treatment began during the second trimester and proceeded without major fetal complications; however, due to rapid maternal disease progression, cesarean delivery at 30 weeks was performed and resulted in the birth of a healthy newborn.[193] In the other patient, crizotinib was initiated in the second trimester and maintained until

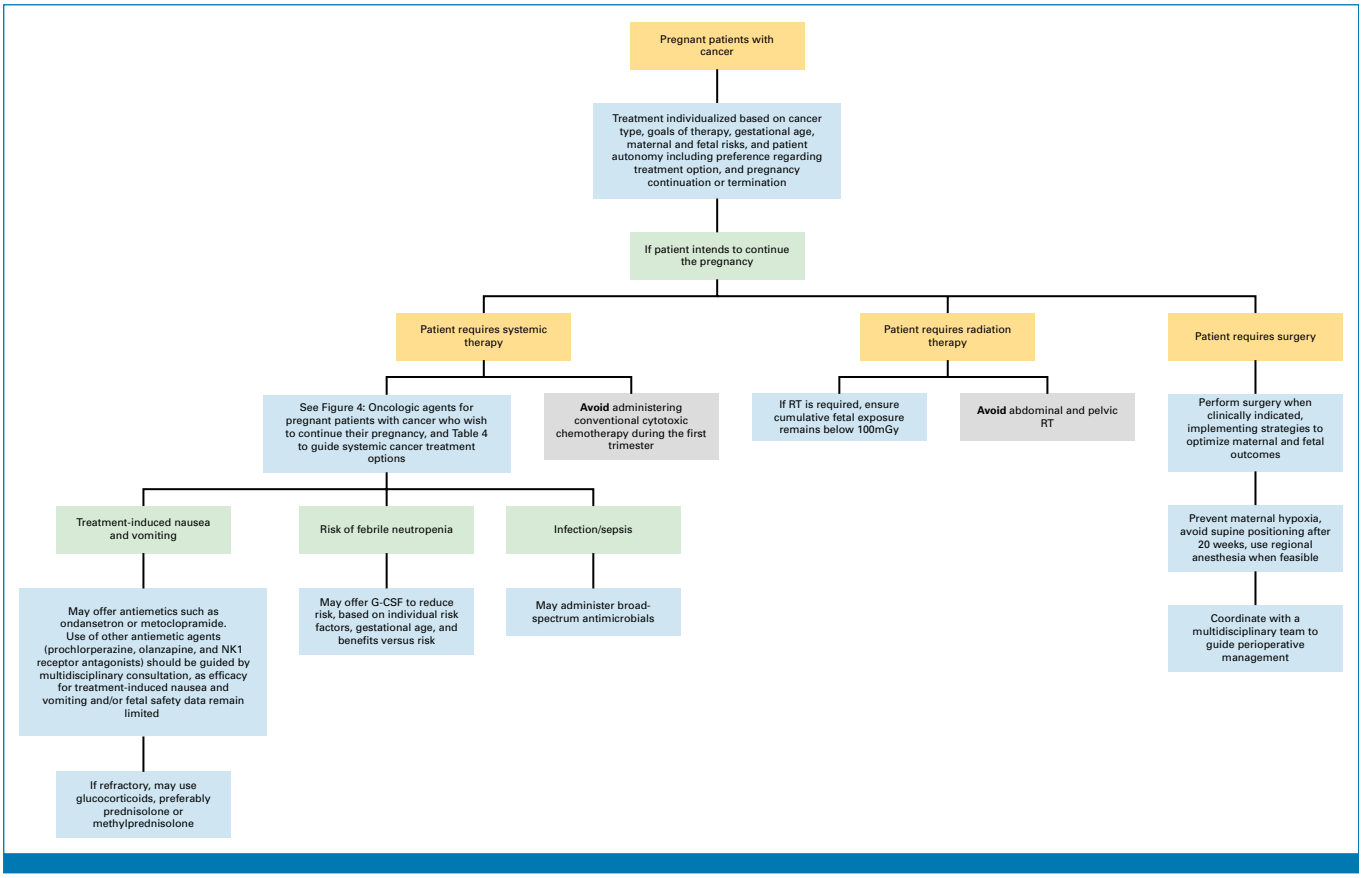

FIG 3. Oncologic management for pregnant patients with cancer. G-CSF, granulocyte colony-stimulating factor; NK-1, neurokinin-1; RT, radiation therapy.

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Oncologic Agents	First Trimester	Second Trimester	Third Trimester
Alkylating agents		**May administer:** Alkylating agents such as cyclophosphamide, ifosdamide, or dacarbazine	
Antimetabolites		**May administer:** 5-fluorouracil and capecitabine, with *DPYD* genotype-guided treatment modification when indicated, or gemcitabine. *Before initiating fluoropyrimidine chemotherapy, offer genetic testing to identify those with DPD deficiency due to genetic variations in the* DPYD *gene, to mitigate the risk of serious adverse reactions.*	
	Do not administer: Methotrexate		
Platinum agents		**May administer:** Platinum agents such as carboplatin, cisplatin, or oxaliplatin *Carboplatin preferred over cisplatin*	
Anthracyclines		**May administer:** Anthracyclines such as doxorubicin, epirubicin, or daunorubicin	
	Do not administer: Idarubicin		
Topoisomerase inhibitors		**May administer:** Topoisomerase inhibitors such as irinotecan or etoposide	
Vinca alkaloids		**May administer:** Vinca alkaloids such as vincristine, vinblastine, or vinorelbine	
Taxanes		**May administer:** Taxanes such as paclitaxel or docetaxel	
Hormonal therapy	**Do not administer:** Tamoxifen, aromatase inhibitors, or GnRH agonists		
HER2-targeted therapy	**Do not administer:** HER2-targeted therapies such as trastuzumab, pertuzumab, lapatinib, or neratinib		
VEGF-/VEGFR-targeted therapy	**Do not administer:** VEGF inhibitors such as bevacizumab, ramucirumab, or aflibercept		
EGFR-targeted therapy		**May administer:** EGFR-targeted TKIs such as erlotinib, gefitinib, afatinib, or osimertinib	
	Do not administer: Cetuximab		
ALK-targeted therapy	**Do not administer:** ALK-targeted therapies such as crizotinib or alectinib		
ABL TKIs		**May administer:** ABL-targeted TKIs such as imatinib or nilotinib	
	Do not administer: Dasatinib		
CD20-targeted therapy		**May administer:** CD20-targeted agents such as rituximab *With close monitoring for fetal development and neonatal hematologic abnormalities*	
MEK and RAF inhibitor therapy		**May administer:** BRAF-targeted TKIs such as vemurafenib	
	Do not administer: MEK inhibitors such as trametinib		
ADCs	**Do not administer:** ADCs such as trastuzumab emtansine, trastuzumab deruxtecan, sacituzumab govitecan, mirvetuximab soravtansine, tisotumab vedotin, enfortumab vedotin, datopotamab deruxtecan, or brentuximab vedotin		
Immune checkpoint inhibitors (CTLA-4 and PD-1/PD-L1 inhibitors)	**Do not administer:** Checkpoint inhibitors such as ipilimumab, nivolumab, and pembrolizumab		
		If checkpoint inhibitor use is essential, restrict to 12-32 weeks of gestation	
Interferon-α	**May administer:** Interferon-α for chronic myeloid leukemia		
PARP inhibitors	**Do not administer:** PARP inhibitors		
Other neoplastic therapies	**Do not administer:** Cellular therapies, hematopoietic cell transplant, and radiopharmaceuticals		

FIG 4. Oncologic agents for pregnant patients who wish to continue their pregnancy. ABL, Abelson tyrosine kinase; ADC, antibody-drug conjugate; ALK, anaplastic lymphoma kinase; BRAF, v-Raf murine sarcoma viral oncogene homolog B1; CD20, cluster of differentiation 20; CTLA-4, cytotoxic T-lymphocyte antigen 4; DPD, dihydropyrimidine dehydrogenase; EGFR, epidermal growth factor receptor; GnRH, gonadotropin-releasing hormone; HER2, human epidermal growth factor receptor 2; MEK, mitogen-activated protein kinase; PARP, poly (ADP-ribose) polymerase; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor; VEGFR, vascular endothelial growth factor receptor.

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delivery at 26 weeks due to maternal complications; the infant was born without malformations.[194] Collectively, these reports suggest that alectinib and crizotinib may be associated with favorable short-term neonatal outcomes when used during pregnancy. However, data remain extremely limited, and the absence of long-term follow-up precludes any conclusions regarding developmental safety or rare adverse effects.

Abelson tyrosine kinase–targeted therapy. Imatinib remains the most extensively studied TKI, with multiple case series and expanded analyses describing maternal and fetal outcomes. Evaluations of drug concentrations in maternal blood, umbilical cord blood, and placental samples collected during labor suggests limited placental transfer.[195] An early review of 180 pregnant individuals reported mostly live births, yet documented a range of congenital anomalies, particularly skeletal malformations (eg, hemivertebra) and, in some instances, renal agenesis.[196] Additional evaluations that consolidate data from primary sources confirm that, although the majority of imatinib-exposed pregnancies do not result in severe malformations, congenital anomalies have been reported.[197,198] However, several reports describe successful outcomes following continued imatinib use throughout pregnancy or after drug discontinuation upon confirmation of pregnancy, particularly when molecular remission had been achieved.[195,199-204] Despite some favorable outcomes, the variability in fetal effects and placental transfer warrants caution, and imatinib is not recommended during the first trimester unless no alternatives are available.[205-207]

Nilotinib exposure during pregnancy, particularly in the first trimester, has raised concerns due to embryotoxicity observed in animal studies; however, human data suggest that limited short-term exposure may not be associated with a high risk of congenital anomalies. Nilotinib appears to have limited placental transfer and may carry a lower teratogenic risk based on animal studies and emerging human data.[208] Registry and case-based reports also suggest that nilotinib exposure in the second or third trimester may be associated with favorable fetal outcomes, although isolated congenital anomalies have been observed.[195,199,205,209] Nonetheless, nilotinib is to be avoided during organogenesis. In contrast, dasatinib is associated with a significant fetal risk and is strongly contraindicated at all stages of pregnancy. Reports document high rates of adverse fetal outcomes, including hydrops fetalis, FGR, skeletal malformations, and intrauterine fetal death, even when exposure is limited to the second trimester.[197,200,203,210,211] This is consistent with the high placental transfer and mechanism of action of dasatinib that may interfere with fetal development.

CD20-targeted therapy. Rituximab use after the first trimester did not appear to significantly increase the risk of congenital anomalies. Most published cases report live births without structural malformations, although transient neonatal cytopenias, particularly B-cell lymphopenia, have been observed and typically resolve within the first 6 months of life.[212-214] However, prolonged profound hypogammaglobulinemia and class-switching B-cell defects have been reported after in utero rituximab exposure.[215] A systematic review of cancer and autoimmune populations found no consistent pattern of birth defects among exposed neonates. Expert consensus supports rituximab use during the second and third trimesters when clinically necessary for hematologic malignancies such as lymphoma, with close neonatal monitoring recommended.[87,206,216]

BRAF- and MEK-targeted therapy. Vemurafenib has shown minimal placental transfer in animal models, and available human case reports (n = 4) have described its use during the second or third trimester.[217-220] In all reported cases, delivery occurred prematurely between 26 and 36 weeks, with one instance of FGR. However, no major congenital anomalies or persistent neonatal health issues were observed.[217-220] Dabrafenib has demonstrated teratogenicity in animal models at exposures approximately three times those achieved in humans, including embryo-lethality and cardiovascular and skeletal abnormalities.[198]

Mitogen-activated protein kinase (MEK) inhibitors, such as trametinib, have also shown teratogenic effects in preclinical studies, and no human data currently support their safety in pregnancy.[86]

Antibody-Drug Conjugates

Published data on the use of antibody-drug conjugates (ADCs) during pregnancy are extremely limited, consisting primarily of isolated case reports, conference abstracts, and pharmacovigilance analyses. A single detailed case describes brentuximab vedotin administration with cyclophosphamide, doxorubicin, and prednisone for ALK-negative anaplastic large-cell lymphoma at 15 weeks' gestation, resulting in favorable maternal and neonatal outcomes.[245] In acute myeloid leukemia, gemtuzumab ozogamicin has been administered during the second trimester as part of multiagent chemotherapy, with exposures documented in single-center case series reported only as a conference abstract.[367] Data on trastuzumab emtansine (T-DM1) are extremely limited; however, reports have suggested a potential signal for increased risk of cardiovascular malformations following exposure during pregnancy (reporting odds ratio [ROR], 4.46 [95% CI, 1.02 to 19.52]), although the absolute number of reported cases is small and causality cannot be confirmed.[172] No in-pregnancy case reports were identified for trastuzumab deruxtecan, sacituzumab govitecan, enfortumab vedotin, or mirvetuximab soravtansine. In general, for ADCs, risk assessment should consider both the antibody target (eg, CD30, HER2) and the linked cytotoxic agent (eg, vedotin, monomethyl auristatin E, DM1), as both components may contribute to maternal and fetal toxicity. Given the paucity of data and the potential for harm, the use of ADCs during pregnancy should generally be avoided unless the expected maternal benefit clearly outweighs the risks.

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Immunotherapy

Several studies have described favorable maternal and neonatal outcomes following immune checkpoint inhibitor (ICI) treatment during pregnancy, particularly with monotherapy. Ipilimumab, nivolumab, and pembrolizumab monotherapy administered after the first trimester leads to disease control and delivery of healthy infants in most cases.[221-223] Combination therapy (nivolumab + ipilimumab) has been associated with preterm but uncomplicated deliveries.[224-226]

Adverse events were also documented. Combination ICI exposure during mid-gestation has been linked to extreme prematurity with neonatal complications, including respiratory distress, intraventricular hemorrhage, retinopathy of prematurity, and transient congenital hypothyroidism.[227,228] Nivolumab exposure was reported in a twin pregnancy that required a preterm delivery at 30 weeks due to the development of hemolysis, elevated liver enzymes, and low platelets syndrome. One twin was born with a congenital limb defect attributed to amniotic banding rather than ICI exposure, while the other twin was born without anomalies.[229] A severe case following pembrolizumab exposure beginning at 16 weeks and extended beyond 32 weeks led to immune-mediated neonatal enterocolitis at 4 months, which required corticosteroids, infliximab, and prolonged hospitalization.[230]

Pharmacovigilance analyses echoed this variability. A VigiBase study of 91 reports of ICI exposures during pregnancy found no increased rates of preterm birth, spontaneous abortion, or congenital malformation compared with other anticancer drugs.[232] However, combination ICI therapy was significantly associated with preterm birth (80% *v* 23%; ROR, 13.87 [95% CI, 3.90 to 49.28]; $P < .001$), and spontaneous abortion was the most frequently reported complication (31%). Another pharmacovigilance study of 46 ICI-exposed pregnancies with available outcome data reported spontaneous abortion in 23% of ICI-exposed pregnancies, elective termination in 17%, and preterm birth in 37%.[231]

Although these reports suggest that most ICI-exposed pregnancies result in healthy outcomes, the limited number of cases, potential underreporting, positive-result publication bias, and lack of long-term follow-up constrain definitive conclusions.

Cellular Therapy

There are no data on the use of chimeric antigen receptor (CAR) T-cell therapy in pregnancy, and no animal studies have been conducted to assess its potential for fetal harm.[368,369] However, based on the mechanism of action, if transduced cells cross the placenta, fetal toxicity may occur.[234,368,369] Therefore, CAR T-cell therapy is contraindicated during pregnancy.[370]

Hematopoietic cell transplantation, even with reduced intensity or nonmyeloablative conditioning regimens, is contraindicated during pregnancy.[371]

Interferon

Interferon-alpha (IFN-α) has limited placental transfer due to its large molecular weight and has not been associated with fetal malformations, even when used in the first trimester.[197,200,246,247] As a result, IFN-α is considered relatively safe and can be used throughout pregnancy.

PARP Inhibitors

Poly (ADP-ribose) polymerase (PARP) inhibitors, such as olaparib, niraparib, talazoparib, and rucaparib, have demonstrated teratogenicity in animal studies, with findings including skeletal abnormalities, growth restriction, and fetal demise at clinically relevant exposures.[180,233] These adverse effects are attributed to interference with DNA repair mechanisms, which are essential for organogenesis. As a result, PARP inhibitors are contraindicated during pregnancy, and individuals of reproductive potential are advised to use effective contraception during treatment and for a period following discontinuation.[233] Human data are exceedingly limited, and a recent review found no published cases of in utero PARP inhibitor exposure in patients with cancer.[233] This absence is likely due to exclusion from clinical trials and adherence to the existing safety guidelines. Overall, the quality of evidence on PARP inhibitors is very low, but based on current evidence and mechanistic rationale, existing expert consensus supports the avoidance of all PARP inhibitors during pregnancy.[180]

Radiation Therapy

Evidence regarding the safety and outcomes of RT during pregnancy is primarily derived from retrospective studies, case reports, and expert opinion, with limited availability of high-quality prospective data.[8,248,249] Findings suggest that fetal radiation exposure should generally not exceed a cumulative dose of 100 mGy, as doses above this threshold have been associated with dose-dependent neurodevelopmental effects, including intelligence quotient (IQ) reduction and severe intellectual disability.[1,8,12,248-253]

The first trimester, particularly the organogenesis period (2-7 weeks gestation), appears to be the most sensitive window for fetal anomalies or pregnancy loss due to radiation exposure.[249,253,254] Evidence indicates an increased risk of congenital malformations, small head size (SHS), IUGR, and cognitive impairment when embryonic or fetal doses exceed 100 mGy.[250,255] Doses exceeding 300 mGy are associated with a significantly higher incidence of neurocognitive impairment.[256] RT during this period carries an increased risk of spontaneous abortion and fetal death,[250] and is therefore rarely used in clinical practice. However, with rigorous dosimetric planning, early pregnancy RT may be feasible in

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carefully selected patients. One case involving intraoperative RT (IORT) for a brain metastasis during early gestation reported a uterine dose of <0.5 mSv and a healthy delivery at 32 weeks.[257]

During the second trimester, fetuses demonstrate greater resistance to teratogenic effects of radiation but are more susceptible to neurodevelopmental effects. Nonetheless, fetal proximity to radiation fields increases with gestational age, and second-trimester exposure has been associated with risks such as growth restriction, SHS, cataracts, and sterility.[249,250,258] Whole-breast irradiation, when performed in the second trimester, has been reported to result in fetal doses below 50 mGy.[259,260] In a longitudinal study of 43 children exposed in utero to extra-abdominal and extrapelvic RT, normal neurocognitive development was observed in 77% of children, with median age at first assessment 3 years and median age of last assessment 12 years, although the findings remain limited by cohort size and study design.[372] Favorable long-term pediatric outcomes have also been reported following RT for oropharyngeal cancer during the second trimester,[262] supporting the feasibility of carefully planned treatment during this period.

By the third trimester, fetuses are less vulnerable to teratogenic effects of radiation, and exposure to radiation is less frequently associated with adverse developmental outcomes. Studies suggest that doses below 500 mGy during this period are not currently associated with a significant increase in the risk of cognitive impairment, although the potential for preterm labor induced by RT has been reported.[250,263,264] The estimated risk of radiation-induced childhood cancer is also markedly lower following third-trimester exposure compared with earlier gestational periods.[265]

Clinical case series have reported the successful administration of RT during the second and third trimesters for various malignancies, including Hodgkin lymphoma and non-Hodgkin lymphoma, breast cancer, and head and neck tumors. Fetal doses ranging from 14 to 55 mGy have been reported for supradiaphragmatic RT in Hodgkin lymphoma, with no observed neonatal complications or congenital malformations.[120,272] Similarly, fetal exposures below 100 mGy have been achieved in patients with breast and head and neck cancers treated during early to mid-pregnancy, particularly when intraoperative boosts or advanced treatment planning techniques are employed.[1,254] Modern approaches, such as intensity-modulated proton therapy, are better at reducing fetal exposure to radiation compared with 3D conformal RT and volumetric-modulated arc therapy while maintaining effective maternal tumor control.[266,269] In contrast, pelvic RT for gynecologic malignancies during pregnancy is consistently associated with substantial fetal risks, including spontaneous abortion and severe fetal harm, and is generally avoided.[249,250]

Advances in RT techniques, including IORT and the use of proton or electron beams, have enabled significant reductions in fetal radiation exposure.[249,250,267,268] IORT used during breast cancer treatment at 15 weeks' gestation resulted in a reported fetal dose of 0.84 mGy.[273]

Fetal shielding has been shown to decrease exposure during photon-based RT, although it may be less effective with proton therapy.[1,269-271] Individualized treatment planning, including optimized beam angles, field design, and shielding, can significantly reduce fetal dose.[267] Despite certain logistical and dosimetric limitations, proton therapy may offer advantages in pregnancy due to its steep dose gradients and minimal exit dose, making it particularly beneficial for treating deep-seated tumors.[269]

Surgery

Evidence indicates that surgery can be performed safely during pregnancy across all trimesters when managed by experienced multidisciplinary teams, although the early second trimester is often considered the most favorable time for intra-abdominal procedures.[274] The safety of surgical interventions is supported by moderate-quality observational data, with fetal risk mitigated through the appropriate use of anesthesia and fetal monitoring.[275]

Studies have shown that both laparoscopic surgery and laparotomy have been utilized during pregnancy, with the choice being influenced by gestational age, procedural complexity, and surgeon experience. Locoregional anesthesia is often preferred over general anesthesia to reduce fetal exposure,[274] although general anesthetic agents have generally been used without adverse fetal outcomes.[10] Evidence suggests that maintaining intraperitoneal pressures at or below 15 mmHg and limiting procedural time to < 90 minutes may reduce fetal and maternal complications.[137,274]

Surgical approaches vary significantly according to cancer type, stage, location, and gestational timing. Therefore, clinicians are encouraged to refer to site-specific guidelines and multidisciplinary team recommendations for detailed, evidence-based management plans tailored to individual patients. For breast cancer, modified radical mastectomy and breast-conserving surgery, including SLNB using radiocolloids, have been performed safely throughout pregnancy.[6,62,276,277] However, the use of blue dye in SLNB remains controversial due to limited data on fetal safety and the risk of maternal anaphylaxis, and technetium-99m is preferred to mitigate this risk.

In gynecologic cancers, procedures such as cone biopsy or simple trachelectomy for early-stage cervical cancer have been performed up to 22 weeks of gestation, although there is a risk of bleeding, especially if performed after the first trimester, and a risk of preterm birth.[8,278-284] For ovarian cancer, laparoscopy has been safely used for staging.[8,285-287] In early-stage disease, conservative surgery during pregnancy followed by definitive staging post-delivery is frequently reported.[8,288-290] In advanced-stage ovarian cancer with peritoneal spread, available evidence supports approaches such as pregnancy termination or neoadjuvant

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chemotherapy before 22 weeks, with delayed postpartum surgery.[8,162,180]

For thyroid cancer, surgery is reported to be safe throughout gestation; second-trimester intervention will minimize risks related to maternal hypothyroidism and fetal development.[291] Gastric cancer management during pregnancy generally follows protocols used in nonpregnant patients.[83,292-294] Evidence supports the use of endoscopic resection for early-stage disease prior to 22 weeks' gestation, which maintains the pregnancy,[292,293] while gastrectomy may be required for advanced disease based on TNM staging and tumor location.[292,294] For pregnant patients diagnosed with a localized renal mass, surgical management may be an option.[295-297] When diagnosis occurs in the late third trimester, delivery should be planned to avoid treatment delays.[295,296] For melanoma, data support the safety of skin biopsies and wide local excisions throughout pregnancy.[86,298] SLNB using radiocolloids has also been utilized during pregnancy without adverse fetal outcomes.[86,298]

Despite favorable safety profiles, surgical interventions during pregnancy are associated with risks, such as preterm labor, fetal distress, and miscarriage.[1] Maternal physiologic changes during pregnancy, including an increased risk of aspiration due to gastroesophageal reflux, necessitate careful perioperative management.[137,299] Maintenance of adequate maternal oxygenation and hemodynamic stability is essential to preserving uteroplacental perfusion.[137,299]

Pain management in the postoperative period remains a clinical challenge due to limited analgesic options. Evidence indicates that inadequate pain control may contribute to uterine contractions and preterm labor.[137] Nonsteroidal anti-inflammatory drugs (NSAIDs) are contraindicated after 28 weeks due to the risk of premature ductus arteriosus closure,[137] whereas brief courses of narcotics are generally well tolerated by fetuses.[300] Consultation with anesthesia specialists is essential to ensure the safety of both the patient and her fetus.

Supportive Care

Antiemetics

The safety of antiemetic agents used during chemotherapy during pregnancy has been assessed primarily through observational cohort studies, registry-based analyses, and systematic reviews. Among these agents, ondansetron and metoclopramide have been the most extensively studied.

Several population-based cohort studies have examined the association between ondansetron exposure and congenital anomalies. Some retrospective studies have reported potentially increased risk of specific defects, particularly oral clefts, cardiac septal defects, and renal agenesis, when exposure occurs during the first trimester.[301-304] However, other large observational studies found no association between ondansetron and an increased risk of major congenital malformations, stillbirth, spontaneous abortion, or fetal death when compared with other antiemetics.[305-308] Systematic reviews have similarly concluded that the absolute risk of adverse fetal outcomes related to ondansetron exposure in early pregnancy appears to be low, despite some variation in findings across studies.[309,310]

Metoclopramide has also been evaluated in pregnancy in multiple cohort studies. These studies reported no statistically significant increase in major congenital malformations or fetal loss following exposure.[311,312] Adverse effects related to dopaminergic blockade, such as extrapyramidal symptoms, have been reported with prolonged use,[313,314] although these have not been systematically quantified in pregnancy cohorts.

Prochlorperazine is commonly used to treat nausea during pregnancy; however, there is a lack of high-quality data evaluating its safety. No major population-based or prospective studies reporting congenital or obstetric outcomes associated with prochlorperazine were identified in this review.

Clinical safety data in pregnancy are limited for neurokinin-1 (NK1) receptor antagonists, including aprepitant and fosaprepitant.[368,369] No prospective cohort studies or randomized controlled trials evaluating fetal or neonatal outcomes associated with NK1 antagonists have been identified. These agents were classified as US Food and Drug Administration (FDA) category B, based on preclinical data. Since 2015, the FDA removed pregnancy letter categories from the labels and also requires the labels to be updated when information becomes outdated. The FDA replaced the letter category with a more detailed narrative to assist health care providers in assessing benefit versus risk.

Olanzapine, an atypical antipsychotic with antiemetic properties, has been studied in the context of mental health disorders during pregnancy. A prospective cohort study including 561 women exposed to second-generation antipsychotics reported no overall increase in spontaneous abortion, stillbirth, or major congenital anomalies; however, a higher rate of atrial and ventricular septal defects was observed in comparison with a cohort of 1,122 patients using drugs not known as harmful.[315] Other studies on olanzapine exposure during pregnancy have not consistently demonstrated associations with adverse obstetric or neonatal outcomes.[316-318] No studies specifically evaluating olanzapine for chemotherapy-induced nausea and vomiting (CINV) in pregnancy were identified.

Across all drug classes, evidence remains limited for second-generation 5-HT3 receptor antagonists (eg, palonosetron) and newer combination regimens involving NK1 inhibitors or atypical antipsychotics. No randomized controlled trials evaluating antiemetics in pregnant patients with cancer were identified.

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Glucocorticoids for CINV

Glucocorticoids are commonly used in combination with other antiemetic agents to prevent CINV in both pregnant and nonpregnant populations. Evidence indicates that although glucocorticoids are generally considered safe during pregnancy, their pharmacokinetic and pharmacodynamic properties differ by type. Fluorinated glucocorticoids such as dexamethasone and betamethasone readily cross the placenta, whereas nonfluorinated agents such as prednisolone, prednisone, and methylprednisolone undergo significant placental metabolism, resulting in lower fetal exposure.[319,320] Studies have consistently reported limited transplacental passage of nonfluorinated agents, although the comparative safety outcomes between agent types remain underexplored in randomized trials. Nonfluorinated glucocorticoids are preferred over fluorinated agents for the treatment of CINV during pregnancy.

Granulocyte Colony-Stimulating Factor

Prenatal exposure to chemotherapy in the final month of gestation has been associated with transient neonatal neutropenia. One early study reported neutropenia in 33% of neonates exposed within 4 weeks of delivery,[321] while a more recent cohort reported a 20% incidence in neonates delivered 22-28 days after maternal chemotherapy, lower due to the adopted practice of avoiding delivery within 3 weeks of chemotherapy.[322] Maternal chemotherapy-induced neutropenia rates have been documented at 13% for grade 3 to 4 neutropenia and 21% for all grades.[90]

Granulocyte colony-stimulating factor (G-CSF), often used to prevent febrile neutropenia during chemotherapy, can cross the placenta and cause adverse outcomes, such as low birth weight and miscarriages in animal models.[323] However, multiple observational studies have found no significant increase in neonatal or maternal complications with G-CSF use during human pregnancy.[90,158,324-327] In a pooled analysis by the INCIP, outcomes in 42 pregnant patients receiving G-CSF during chemotherapy were comparable to those not exposed.[90] No increased incidence of congenital abnormalities or fetal death was reported in this series. G-CSF in pregnancy should be used only when clearly indicated; moreover, there is no evidence to support its prophylactic use before delivery.[90]

Antimicrobials

Antimicrobials play a role in both preventing and treating neutropenic sepsis and should be prescribed based on the chemotherapy protocol and current clinical guidelines.[328] The literature supports the use of broad-spectrum antimicrobials in cases of sepsis, with careful consideration of choosing agents with established safety profiles.[329,330] Penicillins, cephalosporins, and metronidazole are considered safe during pregnancy.[328,330,331] In cases of prolonged neutropenia, antifungal agents have also been utilized, although data on their safety in pregnancy are limited.[328,332]

Clinical Interpretation for Oncologic Management

Systemic therapy decisions in pregnancy hinge on cancer type and stage, gestational timing, therapeutic urgency, and regimen-specific toxicity. Cancer-directed therapy during the first trimester carries the highest risk for teratogenicity and embryotoxicity except monoclonal antibody–based targeted therapies, which do not cross the placenta before approximately 14 weeks' gestation. Initiation of chemotherapy in the second or third trimester is associated with significantly lower rates of congenital anomalies, although risks such as preterm birth, IUGR, transient neonatal cytopenias, and potential organ-specific toxicities (eg, cardiac, renal) persist and require close surveillance. Many chemotherapy protocols can be used in pregnancy, mirroring standard regimens and dosing in nonpregnant patients. However, regimens with heightened embryotoxic potential (eg, high-dose alkylators, methotrexate, BEACOPP) are generally avoided. *DPYD* testing is recommended in pregnant patients who will receive 5FU or capecitabine. Targeted therapies require individualized benefit-risk evaluation, with imatinib and rituximab representing the most studied agents to date. CDK 4/6 inhibitors should be avoided in pregnancy as there is a paucity of safety data.[6] Immunotherapies, particularly combination ICI regimens, have been associated with both favorable and adverse pregnancy outcomes in small case series, necessitating extreme caution and robust perinatal monitoring. CAR T-cell therapy remains contraindicated in pregnancy, as does hematopoietic cell transplantation. Multidisciplinary collaboration, integrating oncology, maternal-fetal medicine, neonatology, and pharmacology, remains critical to individualized decision making. Ongoing data collection, including prospective registries, well-designed observational studies, and eventual clinical trials, will be critical to advancing our understanding of the long-term impact of these therapies on both maternal outcomes and child development.

RT during pregnancy remains a complex clinical scenario that demands individualized risk-benefit assessment. Cumulative fetal dose should not exceed 100 mGy to minimize risks of neurodevelopmental effects, congenital malformations, and IUGR, particularly during the first trimester's organogenesis period, where doses above this threshold increase risks of spontaneous abortion and cognitive impairments.[1,254] Techniques such as whole-breast irradiation, IORT, and supradiaphragmatic RT in the second or third trimesters achieve fetal doses ≤50-55 mGy, without reported neonatal complications.[120,259,372] Modern techniques such as intensity-modulated radiation therapy, photon shielding, and proton therapy have also enabled safe RT for selected cancers, with fetal doses well below risk thresholds.[1,254,269,373] These techniques offer viable alternatives in carefully selected patients, especially where

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maternal treatment cannot be delayed. However, pelvic RT for gynecologic malignancies is contraindicated during pregnancy due to unavoidable high uterine dose and high risks of fetal harm and spontaneous abortion.[249,250,269] Therefore, when RT is necessary, multidisciplinary planning should prioritize RT in the second or third trimester, strictly adhering to fetal dose constraints, and selecting nonpelvic targets to ensure effective maternal cancer control while minimizing risks to fetal health.

For the diagnosis, staging, or treatment of cancer, surgery can be performed safely during pregnancy in any trimester in experienced hands with surgeons and anesthesiologists familiar with the physiologic changes during pregnancy and unique pregnancy-related risks. Expert opinion helps guide nuanced decisions (eg, anesthesia choice, SLNB dye selection, multidisciplinary management), particularly where evidence is limited or variable by cancer type or gestational age. However, there remains an increased risks of maternal complications such as aspiration, thromboembolism, blood loss and infection, as well as fetal risks including miscarriage, preterm labor, and distress. Locoregional anesthesia is preferred, although general anesthesia is not contraindicated. SLNB can be performed with radio colloids in all nonpelvic cancers, while indocyanine green is preferred for pelvic cases. Maintenance of adequate maternal oxygenation and hemodynamic stability is essential to preserving uteroplacental perfusion, and fetal monitoring should be considered after fetal viability when feasible. Postoperatively, brief courses of opioids are appropriate at any gestational age, while NSAIDs may be used up to 28 weeks; inadequate pain control is linked to uterine contractions and preterm labor.

Recommendations for supportive care for pregnant patients receiving cancer therapy are overall similar to those in nonpregnant people with cancer. Importantly, supportive measures should not be withheld for safety concerns. When corticosteroids are required to augment antiemetic therapy, nonfluorinated agents such as prednisone and methylprednisolone are preferred to minimize fetal exposure. While indwelling central venous catheters should be avoided when possible, during pregnancy due to infection and thrombosis risk,[374] their use may be necessary for safe administration of systemic therapy and should be accompanied by appropriate counseling.

OBSTETRICAL MANAGEMENT

Literature Review and Analysis

The systematic review identified 113 studies that met the inclusion criteria, serving as the evidentiary foundation for current best practices in obstetrical management for patients with cancer. A total of 16 studies covered delivery planning,[1,8,9,64,97,102,322,357,375-382] eight fetal monitoring and growth restriction,[8,9,64,88,383-386] 46 postpartum care,[161,251,299,322,323,328,377,383,387–400,401-424] and 31 reported on long-term effects on offspring.[11,64,87,88,91,101,107,132,261,322,383,393,408,425-442] An additional 24 studies focused on psychosocial management.[68,443-465] The overall quality of evidence informing obstetrical management in pregnant patients with cancer is generally moderate, based on consistent findings from observational studies across multiple settings. However, for certain aspects, including placental evaluation, the evidence remains limited and of lower quality.

Delivery Planning

Evidence from observational studies and meta-analyses suggests that the mode and timing of delivery in pregnancies complicated by cancer are influenced by both oncologic and obstetric considerations. Although vaginal delivery is generally considered feasible, cesarean section is more frequently performed in this population. A meta-analysis demonstrated that individuals with cancer during pregnancy have a significantly increased risk of cesarean delivery compared with controls (relative risk [RR], 1.58 [95% CI, 1.31 to 1.89]), although it remains unclear whether procedures were elective or emergent.[377] These findings may reflect a lower threshold for surgical delivery in the context of maternal or fetal compromise.[377] In particular, cancers involving the cervix or vulva have been associated with a higher use of cesarean delivery.[8,375,376]

Timing of delivery is typically planned around chemotherapy schedules and fetal maturity and coordinated among multidisciplinary specialists, including obstetricians, oncologists, gynecologic oncologic surgeons, and neonatologists.[9,375,376] Current evidence supports aiming delivery at or after 37 weeks of gestation, when feasible, to mitigate complications associated with prematurity.[9,64,375,378] To reduce the risk of maternal and fetal hematologic toxicity, chemotherapy is typically stopped by 34-35 weeks of gestation, with delivery planned 1-3 weeks later depending on the regimen.[1,9,64,322]

Preterm birth is a well-documented complication of cancer-associated pregnancy. Systematic reviews and primary studies have reported significantly increased risks of preterm delivery (adjusted odds ratios [aORs] up to 11.8) and low birthweight (aORs up to 5.5) compared with the general pregnant population.[97,357,377,379,380] A population-based observational study within the adolescent and young adult (AYA) Horizon Study found an increased risk of preterm delivery (prevalence ratio [PR], 2.70 [95% CI, 2.24 to 3.26]); very preterm delivery (PR, 1.74 [95% CI, 1.12 to 2.71]); induction of labor (PR, 1.48 [95% CI, 1.27 to 1.73]); low birth weight (PR, 1.97 [95% CI, 1.55 to 2.50]); and cesarean delivery (PR, 1.18 [95% CI, 1.04 to 1.34]) in cancer diagnosed during pregnancy.[380] Other reports suggest that the incidence of medically indicated preterm birth has decreased over the past two decades,[102] possibly reflecting greater efforts to prolong pregnancy when maternal and fetal conditions permit.

Infants born before 37 weeks are at increased risk of respiratory distress syndrome, neurodevelopmental delay,

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and prolonged hospitalization.[9] Outcomes are particularly poor for those delivered before 28 weeks, with higher rates of bronchopulmonary dysplasia, intraventricular hemorrhage, and necrotizing enterocolitis.[381] Neurodevelopmental impairment and cerebral palsy risk decrease with advancing gestational age, with the risk of prematurity complications falling from 35% at 30 weeks to under 10% at 34 weeks.[381] In addition, preterm infants born to mothers with cancer have a reported higher incidence of neonatal complications compared with the general population (aOR, 2.67 [95% CI, 1.86 to 3.84]), especially when birth occurs before 34-35 weeks.[382] Preterm delivery or termination may be medically necessary when maternal health demands immediate intervention.

Fetal Monitoring and Growth Restriction

FGR is a well-described complication of pregnancies affected by maternal cancer, often due to placental insufficiency or direct effects of chemotherapy.[88,383,384] Chemotherapy administered before 20 weeks' gestation, prolonged chemotherapy exposure, and a maternal diagnosis of acute leukemia have been associated with an increased risk of FGR.[88]

While the optimal frequency for fetal surveillance has not been established in prospective studies, current guidelines advise conducting evaluations every 3-4 weeks beginning at 22-24 weeks of gestation to monitor fetal growth, amniotic fluid levels, and Doppler flow in cases of FGR.[8,9,64,385,386] However, there is limited evidence evaluating the effectiveness or comparative outcomes of different surveillance intervals or modalities in this population.

Postpartum Care

Histologic Evaluation of the Placenta

Six reviews were identified in the literature search that reported on published cases of placental metastases.[387-392] Melanoma (30%), lung cancer (12%), and breast cancer (12%) were the most frequently reported types to metastasize to the placenta.[391]

Placental metastases, although rare, represent significant complications of maternal cancers. Prognosis in patients with placental metastases is generally poor, with one study reporting an 81% mortality rate, largely due to widespread disease.[391] A systematic review of 72 patients identified placental metastases in 84.7% and fetal metastases in 33.3% of patients.[388] Among the patients presenting placental involvement, median maternal survival was 1 month postpartum and an infant 1-year survival rate of 51.1%.[388] In another systematic review of 25 articles, encompassing 489 patients, placental metastases were found to be present in six patients with advanced cancer, representing 1.2% of all the patients included in the review.[389] Another review summarizing 111 studies on placental pathology linked to cancer identified 87 patients with placental invasion by cancer cells, involving the intervillous space and rarely the villous tissue.[391] A review of 93 patients with lung cancer in pregnancy identified from 1953 to 2022 showed that placental examination was conducted in 45 patients, with metastases identified in 35.6%.[392]

Although the quality of evidence supporting histologic evaluation of the placenta in pregnant patients with cancer is generally low, primarily due to the rarity of cases and reliance on case reports and series, available data support consideration of placental examination in all cancer cases diagnosed during pregnancy. This evaluation, ideally conducted by an informed pathologist, may aid in detecting metastatic disease and contribute to patient restaging.[251,391]

Management of Complications

Cancer in pregnancy carries an increased risk for preterm birth and low birth weight even if untreated. Patients who have received chemotherapy within 3 weeks of delivery are at a heightened risk of complications due to potential maternal and transient neonatal myelosuppression, which can increase the susceptibility to delayed wound healing and infection for mother and infant.[322,328,393] Observational data support increased clinical vigilance in this population, particularly for those with hematologic toxicity at the time of delivery who are at risk of postpartum hemorrhage.[161,383] While pharmacologic interventions are often required in the postpartum period, data on medication safety and efficacy in this context remain limited.

Glucocorticoids for Fetal Lung Maturation

A Cochrane review found that a single course of antenatal corticosteroids significantly reduces the risk of perinatal death, neonatal death, and respiratory distress syndrome in pregnant individuals at risk of preterm birth, with probable reduction in intraventricular hemorrhage as well.[394] However, evidence examining long-term neurodevelopmental outcomes remains limited and inconsistent.[395-399] While the Cochrane review reported no conclusive effect on intellectual impairment in childhood (RR, 0.86 [95% CI, 0.44 to 1.69]) or adulthood (RR, 0.24 [95% CI, 0.01 to 4.95]), more recent population-based cohort data identified a modest but statistically significant association between antenatal corticosteroid exposure and increased risks of autism spectrum disorders (adjusted RR [aRR], 1.5 [95% CI, 1.2 to 1.9]), attention-deficit hyperactivity disorder (aRR, 1.3 [95% CI, 1.0 to 1.7]), and mood, anxiety, and stress-related disorders (aRR, 1.5 [95% CI, 1.1 to 2.0]).[396] The absolute risk differences in these studies were small, and interpretation is cautioned in light of potential confounding by indication.

Evidence on repeated courses of corticosteroids has identified associations with reduced fetal growth and neonatal head circumference.[400,401,466] However, follow-up studies have reported no significant differences in physical or

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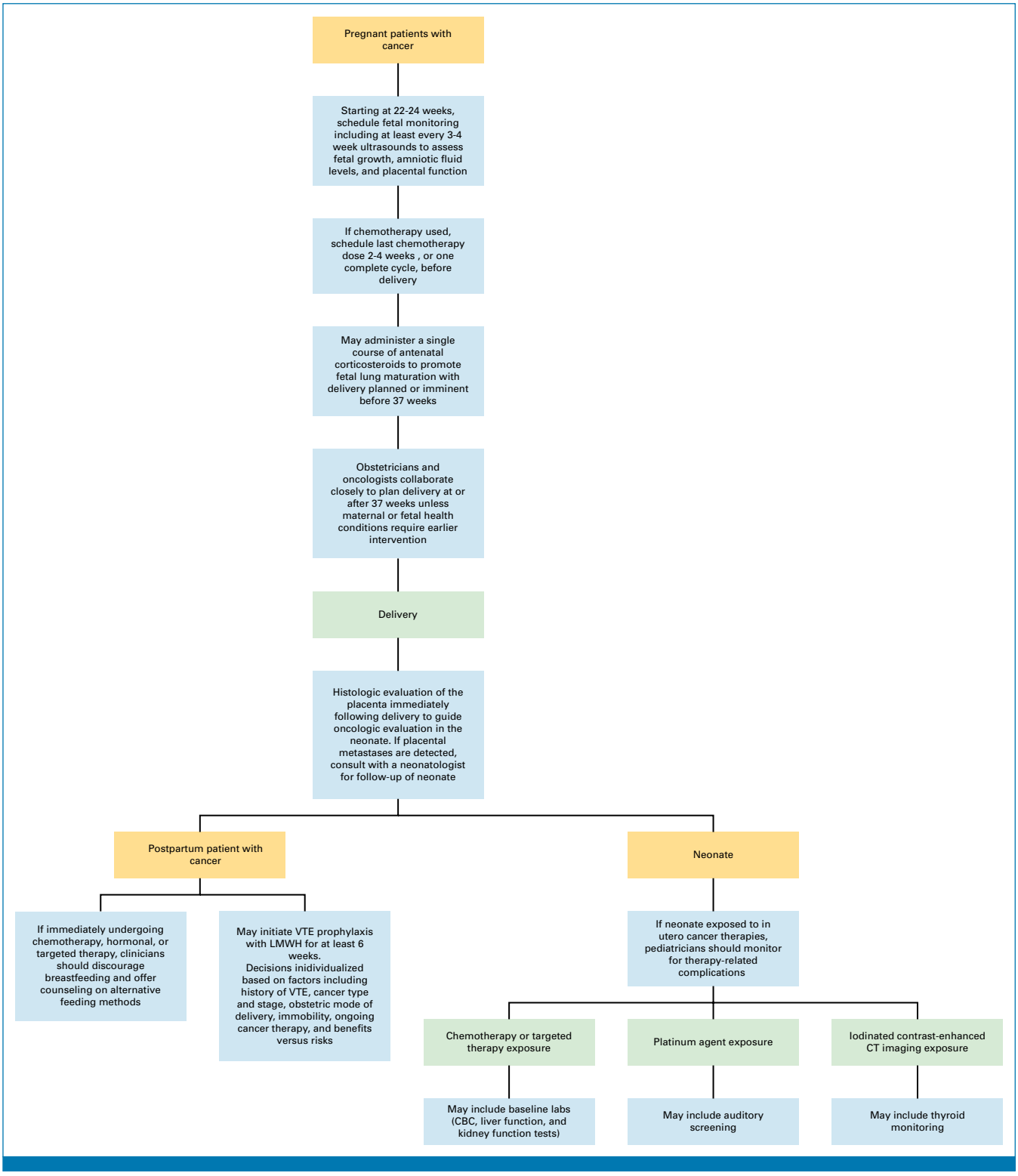

FIG 5. Obstetrical management for pregnant patients with cancer. CBC, complete blood count; CT, computed tomography; LMWH, low molecular weight heparin; VTE, venous thromboembolism.

neurocognitive outcomes at 2 years of age[400,402,466] or in younger children.[404] One study reported a nonsignificant increase in the risk of cerebral palsy (RR, 5.7) following multiple courses of treatment.[403] A Cochrane review pooling data on early childhood cerebral palsy outcomes found no evidence of harm or benefit from repeat dosing (RR, 1.03 [95% CI, 0.71 to 1.49]).[405] Overall, moderate-quality evidence supports the benefit of a single course, while the potential

harm associated with multiple courses remains uncertain. In general, existing guidelines do not recommend serial courses (more than two) of corticosteroids.[299,406,407]

Venous Thromboembolism

Cancer is a well-established risk factor for venous thromboembolism (VTE),[408,409] and evidence suggests that pregnancy further increases this risk. A systematic review and meta-analysis of seven high-quality cohort studies (N = 5,928) found that active malignancy during pregnancy increased the odds of VTE by nearly seven-fold (OR, 6.8 [95% CI, 3.8 to 12.1]).[410] This finding is consistent with that of a separate meta-analysis encompassing 22 studies and over 59,000 pregnancies (RR, 6.78 [95% CI, 5.08 to 8.99]).[377]

Although low molecular weight heparin (LMWH) is commonly used for VTE prophylaxis, especially in the postpartum period, the evidence base for its use during pregnancy is less robust. Available studies indicate that LMWH does not cross the placenta and has a favorable maternal and fetal safety profile.[323] Reports have also documented the successful use of alternative anticoagulants in cases of heparin intolerance,[323] although comparative efficacy and safety data are limited.

Existing evidence emphasizes the need for individualized risk assessment when considering VTE prophylaxis or treatment in pregnant patients with cancer. Guidelines recommend prophylactic use of LMWH be considered in pregnancy if more risk factors such as obesity, pelvic surgery, immobilization and/or hospitalization, peripherally inserted central catheter use, metastatic disease, or compression of blood vessels by tumor or lymph nodes are present.[411,412] Observational studies highlight the importance of balancing thrombotic and hemorrhagic risks, whereas decision-making tools integrating patient preferences may support more personalized care.[409,413,414] However, the effectiveness and clinical utility of these tools in this population have not been systematically evaluated.

Lactation and Breastfeeding

Multiple studies and case reports have documented the presence of chemotherapeutic agents in breast milk following maternal cancer treatment. Platinum-based and nonplatinum alkylating agents have been detected in human breast milk, in some cases persisting for over 3 weeks postexposure.[415-417] The potential for drug transmission to infants has led to widespread reports advising against breastfeeding during active chemotherapy.[417,418]

Alterations in breast milk composition have also been observed in patients with cancer. Studies suggest that both malignancy and chemotherapy can modify the bacterial and metabolic content of breast milk.[419] One observational study found a significantly higher rate of breastfeeding difficulties in women undergoing cancer treatment during pregnancy (63.5%) compared with those not receiving treatment (9%), with earlier gestational age at first chemotherapy cycle and a higher number of cycles associated with increased difficulty.[420] Surgical interventions, particularly breast-conserving surgery, have also been linked to reduced milk production and lobular atrophy.[420]

Evidence-based recommendations for managing lactation in breast cancer survivors and those newly diagnosed with cancer who do not require continued chemotherapy postpartum outline that, in general, a 3-week safety window after the last chemotherapy dose is advised before lactation can safely resume.[251,417,421] While most chemotherapeutic agents are cleared from the body within this time frame, certain drugs (eg, oxaliplatin) require a longer period, hence the need for individualized assessment based on the specific treatment regimen.

Emerging data indicate that breastfeeding may be feasible and safe in selected populations of breast cancer survivors. The POSITIVE trial found that 62.6% of women with hormone receptor–positive breast cancer who gave birth chose to breastfeed, primarily using the contralateral breast (69.2%), with a median breastfeeding duration of 4.4 months.[424] Of these, 37.1% breastfed for 6 months or more. Importantly, during a median follow-up of 41 months, no significant differences in breast cancer recurrence rates were observed between breastfeeding (breast cancer–free interval 1.1% at 12 months) and nonbreastfeeding patients (1.9% at 12 months).[424] Similarly, a cohort study of *BRCA* mutation carriers reported that 23.2% breastfed after treatment, with a median breastfeeding duration of 5 months, and no significant differences in locoregional or contralateral recurrences between breastfeeding (29% 7-year recurrence rate) and nonbreastfeeding women (37%).[422]

A survey of participants of the Young Women's Breast Cancer Study revealed that among those who attempted breastfeeding, 69% had undergone lumpectomy and radiotherapy, with 83% reporting an inability to produce milk from their treated breast.[423] Common reasons for discontinuing breastfeeding included completing the intended duration, initiating or resuming endocrine therapy, and imaging follow-up. Despite physical and treatment-related challenges, 65% reported some level of satisfaction with their breastfeeding experience. A multidisciplinary approach that includes counseling from lactation specialists is essential to guide mothers through potential complications and help them make informed decisions about the safety and practicality of breastfeeding.[9,251,421]

Long-Term Effects on Offspring

Research indicates that children exposed to chemotherapy in utero generally show normal development across various domains, although specific areas such as verbal IQ and emotional control may exhibit subtle differences. The long-term effects of in utero chemotherapy exposure, with evidence from systematic reviews[91,383] and primary studies,[101,107,408,425-432] have demonstrated normal neurologic, cognitive, and cardiac development in children

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exposed to select chemotherapy after the first trimester (Table 5). The included primary studies employed a mix of methodological approaches. Several used epidemiological designs, relying on retrospective medical record reviews or population-based cohorts to assess long-term outcomes.[107,408,426] Others utilized questionnaire-based methods, collecting data through standardized parent or teacher surveys to evaluate behavioral, emotional, and cognitive functioning.[101,425,428,429] A substantial number incorporated direct physical and cognitive examinations, including neuropsychological testing, cardiac assessments, and neuroimaging.[101,107,425-427,429-433]

Cognitive development in exposed children is generally within normal ranges, with no significant impairments in school performance or intelligence reported.[101,428,431] In 57 children of mothers diagnosed with cancer while pregnant, 35 of whom had been exposed to chemotherapy in utero, no significant differences were noted in cognitive ability, school performance, or behavioral competencies between the chemotherapy-exposed group and the unexposed children.[428] Long-term studies assessing children at 6[429,435] and 9 years[434] found only moderate cognitive developmental changes, noting that while full-scale IQ scores were comparable to nonexposed children, verbal IQ scores were slightly lower in those exposed to cancer treatment in utero. However, a significant between-group difference in emotional control was found at 6 years.[435] Despite similar memory, attention, and behavior scores, children exposed to chemotherapy showed lower visuospatial long-term memory scores compared with controls.[429] Emotional regulation and executive functioning are largely unaffected, although weaker emotional control has been noted in some studies.[435]

Neuroimaging studies have shown that prenatal exposure to cancer treatment, particularly platinum-based chemotherapy, can affect local gray and white matter structures, although without disrupting global brain organization or functional connectivity.[427,430] Cognitive outcomes and executive functioning impairments in those with prenatal exposure to chemotherapy were largely associated with prematurity, and this effect is independent of cancer treatment.[383,432]

Several studies have also evaluated the cardiac health of children exposed to potentially cardiotoxic drugs such as anthracyclines.[64,101,107,426,431,433] Most studies reported no structural abnormalities or significant functional impairments.[101,107,425,426,431,433] Some studies noted minor reductions in ejection fraction or elevated diastolic blood pressure, although values generally remained within normal limits.[429,433] The majority of cases with neonatal cardiomyopathy were exposed to idarubicin in utero.

Evidence suggests that children exposed to cisplatin may be at a higher risk of hearing loss, with one study reporting three out of eight exposed children had measurable audiometric deficits.[429] These findings are consistent with earlier case reports.[132] Earlier case reports also support an association between cisplatin and auditory impairment.[132] Standard newborn hearing screens may not detect sensorineural hearing loss, and auditory brainstem response testing has been suggested in such cases.[436]

A number of limitations apply across the studies investigating the long-term effects of in utero chemotherapy exposure. The Avilés studies report favorable long-term outcomes in children exposed to chemotherapy in utero but have been criticized for significant methodological limitations. These include the absence of a control group, reliance on clinical impressions over standardized assessments, and limited detail on outcome measures. Selection and observer bias are likely, and retrospective chart reviews may have missed subtle or delayed effects. Compared with more rigorous prospective studies, the findings may underestimate potential impacts.

Other limitations of the included studies in general involve small sample sizes, which can reduce statistical power and the ability to detect rare or subtle long-term effects. There are inconsistencies in outcome measurement and reporting and confounding variables such as the severity of maternal illness, additional treatments, and factors such as prematurity may obscure the interpretation of outcomes. Additionally, the psychosocial impact of a child growing up in a home where a parent has had cancer and/or where a parent has died further complicates interpretation. There is considerable variability in chemotherapy regimens, including differences in drug types, dosages, and timing of administration, which limits the generalizability of findings. Finally, selection bias is introduced in studies excluding pregnancies that were terminated due to concerns about fetal exposure, potentially skewing outcomes toward healthier cohorts.

Psychosocial Management

The psychological impact of cancer on mental, emotional, social, and spiritual health is well established.[443-446] Elevated rates of anxiety and intrusive thoughts have been documented, alongside unmet informational and practical needs that add to the overall burden of illness.[443,446,447] These challenges are intensified during pregnancy, a time already associated with heightened emotional and psychological vulnerability. Pregnant individuals diagnosed with cancer report higher levels of long-term distress compared with both healthy pregnant individuals and nonpregnant patients with cancer.[447,448]

Qualitative studies highlighted persistent distress, anxiety about fetal outcomes, and difficulties processing medical information related to both oncology and obstetrics.[449,450] One systematic review identified recurring psychological themes in this population, including fear for the baby's health, loss of normal pregnancy experiences, feeling "out of place," and challenges in health care decision making.[450]

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TABLE 5. Studies of Follow-Up of Individuals Exposed to Intrauterine Chemotherapy

First Author (year)	Participants, No.	Median Follow-Up	Summary of Key Findings
Amant (2012)[101]	70 exposed	Children assessed at birth, 18 months, and 5-6, 8-9, 11-12, 14-15, or 18 years. Median follow-up 22.3 months (range, 16.8-211)	In this interim analysis, no increase in CNS, cardiac, or auditory morbidity. Growth and general health normal. There was a significant difference between verbal and performance IQ score in children >6 years of age
Amant (2015)[425]	129 exposed 129 controls	22 months (range, 12-42.0)	No cognitive development differences *v* controls. Normal cardiac evaluation at 36 months (n = 47)
Aviles (2006)[426]	81 exposed	17.1 years (range, 9.3-29.5)	Normal cardiac function and echocardiograms throughout follow-up
Aviles (2012)[437]	54 exposed	22.4 years (range, 3.8-32.0)	Verbal and performance IQ score were within normal range, and academic progress aligned with age, and socioeconomic status
Aviles (2018)[107]	44 exposed	120.4 months (range, 48-299.0)	No clinical malformations were observed, and newborn physiological development showed no evidence of cardiac or neurological damage. Behavior, intelligence, and school attendance were normal. No documented cases of secondary neoplasms or acute leukemia
Blommaert (2020)[427]	42 exposed 42 controls	9.2 years exposed 9.3 years controls	Neuroimaging differences noted with platinum and anthracycline exposure but not correlated with cognitive scores
Blommaert (2019)[432]	20 exposed 20 controls	9.2 years exposed 9.6 years controls	Chemotherapy exposure associated with impaired executive function (response inhibition, spatial attention). These findings were not limited to the effect of late prematurity. Both prematurity and prenatal exposure may have an effect on the development of conflict monitoring
Capozza (2024)[393]	14 exposed 23 controls	12 months	No differences between exposed and unexposed children. Normal auditory brainstem response at 3 months of life in the children exposed to carboplatin. Cardiological and echocardiogram evaluation were normal at birth, 6 months, and 12 months thereafter in the children exposed to anthracyclines. No child born to women with PAC experienced metastasis from the maternal tumor
Cardonick (2015)[428]	35 exposed 22 controls	4.5 years exposed 4.9 years controls (range, 18 months-10.4 years)	No significant differences in cognitive skills, school performance, or behavioral competencies between the chemotherapy-exposed group and the unexposed children. 95% had normal cognitive scores. Older children showed more internalizing behavior symptoms
Finch and Cardonick (2021)[436]	307 exposed	Neonatal follow-up	Higher risk of hearing loss with cisplatin and carboplatin than with oxaliplatin or nonplatinum agents
Garafalo (2016)[438]	22 exposed 38 controls	Neonatal follow-up	Chemotherapy administered during the second trimester or later did not influence intrauterine fetal growth, but SGA common in both exposed and unexposed groups; maternal cancer may contribute to FGR.
Greiber (2022)[408]	42 exposed	14.4 years (IQR, 6.4-25.0)	No increased risk of congenital, somatic, or psychiatric disorders in fetal exposure to maternal cancer and chemotherapy *v* children born to mothers not diagnosed with cancer during or before pregnancy
Gziri (2012)[433]	62 exposed 62 controls	Range, 1-10 years	Lower cardiac function parameters (eg, fractional shortening) in chemo-exposed children. Tissue Doppler and strain measurements were within normal range and not statistically different from normal controls
Hahn (2006)[439]	52 exposed	38.5 months (range, 2-157.0)	Among the 18 school-age children, only two required special education attention: one due to ADHD and another due to Down syndrome
Huis in 't Veld (2025)[431]	122 exposed	12-15 years	Cardiac function, neurocognitive outcomes, including intelligence, memory, and attention were within normal limits. Nine children had lower verbal memory scores linked to chemotherapy exposure (P = .044). Pubertal development was within standard ranges, with no significant associations found between chemotherapy exposure and puberty onset.
La Nasa (2019)[322]	135 exposed	At birth	Chemotherapy within 22-28 days of delivery increased the risk of neonatal neutropenia and leukopenia is highest when delivery is <7 days from chemotherapy
Maggen (2021)[87]	54 exposed 19 controls	Neonatal follow-up	High rates of SGA, prematurity, and neonatal complications among infants born to mothers with non-Hodgkin lymphoma; however, this could not exclusively be explained by the receipt of antenatal chemotherapy
Maggen (2022)[88]	201 exposed	Neonatal follow-up	FGR common after prenatal chemotherapy, with timing and duration being critical factors
Maxwell (2021)[440]	17 exposed 17 controls	4.4 years (range, 3.5-7.0) exposed 3.7 years (range, 3.6-7.0) controls	FSIQ in exposed children confounded by prematurity and maternal IQ. Term infants had normal development. Both groups were comparable in developmental milestones, pediatric anthropometric measurements, and health issues, with no cases of autoimmune cytopenia
Metcalfe (2025)[441]	142 exposed 1,008 controls	Range, 1-15 years	Chemotherapy increased risk of neonatal morbidity and mortality (RR, 1.67), mediated by preterm birth. No increase in long-term disability

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TABLE 5. Studies of Follow-Up of Individuals Exposed to Intrauterine Chemotherapy (continued)

First Author (year)	Participants, No.	Median Follow-Up	Summary of Key Findings
Murthy (2014)[442]	50 exposed	7 years (range, <1-22)	Some delays in early development and learning reported; no significant cognitive abnormalities overall
Passera (2019)[430]	21 exposed	18 months	No differences in brain volumes or early neurodevelopment. No correlation between neurodevelopmental outcome and cumulative dosage of epirubicin administered
Van Assche (2024)[261]	144 exposed	1.5-18 years	In this *interim analysis*, paclitaxel exposure linked to lower visuospatial and verbal memory than docetaxel
Van Assche (2023)[434]	151 total (109 exposed)	9.3 years (range, 7.8-10.6)	No associations between FSIQ and the type of chemotherapeutic agent, exposure level, or timing of exposure during pregnancy
van Gerwen (2021)[11]	755 exposed	Neonatal follow-up	Chemotherapy exposure before 12 weeks of gestation was significantly associated with a higher rate of major congenital malformations (21.7%, OR, 9.24 [95% CI, 3.13 to 27.30]) *v* 3.0% (95% CI, 1.9 to 4.6) after 12 weeks, comparable to rates in the general population
van Gerwen (2020)[435]	37 exposed 37 controls	6 years (range, 5.3-7.0)	In this interim analysis, executive functioning was within normal limits; however, emotional regulation was reduced in exposed children
Vandenbroucke (2020)[429]	132 exposed 132 controls	6 years (range, 4.7-7.9)	Although within normal ranges, statistically significant reduction in verbal IQ and visuospatial memory. Higher diastolic BP observed *v* controls

Abbreviations: ADHD, attention-deficit hyperactivity disorder; FGR, fetal growth restriction; FSIQ, Full-Scale IQ; OR, odds ratio; PAC, pregnancy-associated cancer; RR, relative risk; SGA, small for gestational age.

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Coping styles also influences psychological outcomes; in one cohort, couples using internalizing strategies reported significantly higher levels of concern across domains related to fetal health, maternal illness and treatment, and pregnancy and delivery outcomes, compared with those using other coping strategies.[451]

The compounding stress of cancer during pregnancy may contribute to adverse obstetric and neonatal outcomes, including spontaneous abortion, preterm labor, and growth restriction,[465] as well as cognitive, behavioral, and emotional difficulties in offspring.[452-454] These findings underscore the need for timely, structured mental health support and the importance of including caregivers in psychosocial care to help families navigate practical and emotional burden.[455] Evidence suggests that assigning a dedicated midwife within the multidisciplinary team may strengthen the mother-infant bond and support family formation, including the involvement of partners and access to psychological support. Social workers can help reduce the family burden associated with maternal sick leave, partner caregiving responsibilities, and financial stressors.[68]

Psychosocial care is recognized as a critical component of comprehensive cancer care.[445,456] Although general psychosocial interventions in oncology patients have demonstrated beneficial effects on mood, immune parameters, and, in some cases, survival,[457-459] evidence-based interventions specifically tailored to pregnant patients with cancer and their families remain limited. A scoping review found no formal supportive care or educational programs for pregnant individuals with cancer and their partners.[463] Similar gaps were noted in qualitative interviews, where participants revealed a strong desire for peer support, but participants reported feeling isolated due to the rarity of their condition and a lack of tailored resources.[449,460] The experience of not "fitting in" with either the oncology or maternity care setting was commonly linked to distress.[450,460] Nevertheless, many expressed interest in providing peer support in the future, indicating the potential for structured peer programs to address this gap.[460]

Psychosocial assessment tools validated in the general oncology setting, such as the Distress Thermometer, Edmonton Symptom Assessment System, and structured problem checklists, are commonly recommended.[461] ASCO guidelines recommend routine screening for anxiety and depression in adults with cancer using validated instruments, with symptom severity guiding a stepped care approach to management.[456] The ASCO Consensus Guideline on Patient-Clinician Communication further highlights the importance of structured, empathetic dialogue to support effective psychosocial assessment and patient-centered care.[462] While these frameworks are not pregnancy-specific, they are adaptable to the perinatal oncology context.

Longitudinal data examining the lasting psychological and relational effects of cancer diagnosed during pregnancy remain limited. Studies evaluating the long-term psychological and relational effects on mothers, partners, and children are urgently needed.[463,464] Interventions that incorporate the perspectives of partners and family members, and that address systemic barriers to psychosocial care, will be essential in improving quality of life and psychosocial outcomes for this unique patient population.

Clinical Interpretation for Obstetrical Management

Mode and timing of delivery should be a multidisciplinary decision between obstetrics, MFM, and oncology, and is generally based on both obstetrical and oncologic considerations. When maternal prognosis, treatment urgency, or cancer progression jeopardize maternal health or survival, termination of pregnancy may be medically indicated in earlier gestation, while in later gestation, patients may consider preterm delivery. Generally, vaginal delivery should be considered, with the exception of patients with cervical, vaginal, or vulvar cancer, in which tumor involvement may preclude vaginal delivery. Also, concern for perineal trauma in areas with tumor may influence the safety of vaginal delivery. Timing of delivery should account for chemotherapy cycles, with treatment paused approximately 2-4 weeks, or one complete cycle, before birth to minimize fetal and maternal toxicity. Postpartum chemotherapy can resume within a few days of vaginal delivery or within 1-2 weeks of cesarean section, once healing is adequate.

Pregnant patients undergoing treatment for cancer are at risk for FGR, especially when undergoing treatment in the second or early third trimester. Monitoring for FGR with serial ultrasounds assessing estimated fetal weight is needed starting in the mid second trimester or just prior to the initiation of chemotherapy and continued every 3-4 weeks or prior to each subsequent cycle of chemotherapy. If FGR develops, initiate weekly assessments of amniotic fluid volume, antenatal testing (either nonstress test or biophysical profile) and umbilical artery Dopplers to guide delivery timing. This monitoring will determine whether significant fetal compromise should lead to preterm delivery.

Placental metastases, although rare, carry implications for maternal staging and neonatal risk, especially in advanced systemic or high-risk malignancies such as melanoma, lung cancer, and breast cancer. While metastases typically localize to the maternal intervillous space, fetal involvement via transplacental transmission has been described and is associated with a high neonatal mortality. Given that placental appearance may be normal despite the presence of microscopic disease, placental histopathologic assessment should be considered in all pregnancies complicated by maternal malignancy. Close coordination with MFM and neonatology is advised if placental metastases are identified.

Cancer in pregnancy presents significant risks, including preterm birth, low birth weight, infection, and hemorrhage, particularly if chemotherapy is given within 3 weeks of delivery. Antenatal corticosteroids remain the standard of care for promoting fetal lung maturation in patients at risk of preterm delivery, including those with cancer. A single course reduces the incidence of neonatal respiratory distress syndrome, intraventricular hemorrhage, and neonatal death. Prednisone and methylprednisolone are preferred over dexamethasone for supportive care during pregnancy because they are broken down by the placenta, limiting fetal exposure. Dexamethasone crosses the placenta more easily and should be avoided when safer alternatives are available. Existing guidelines recommend limiting corticosteroid administration to a single course or, at most, one repeat course, and only when strongly indicated. Pregnancy and cancer are independently prothrombotic states, and their combination significantly elevates the risk of VTE. LMWH remains the anticoagulant of choice due to its safety profile, lack of placental transfer, and ease of monitoring. However, limited high-quality evidence exists to guide dosing and duration in this specific population. Individualized risk assessment is essential when initiating VTE prophylaxis, particularly in the context of potential hemorrhagic complications or peripartum procedural needs. The role of shared decision-making tools remains promising but unvalidated in this population.

The decision to breastfeed depends on patient preferences and feasibility, as well as potential risks of agents transmitted to the infant through breast milk. Considerations include the recency of treatment with systemic agents prior to delivery and their half-lives, as well as the need to undergo further therapy and urgency of that therapy after delivery. If therapy must resume promptly, patients may choose to pump and dump to maintain lactation while preventing infant exposure to systemic agents, with the option of resuming breastfeeding when safe. If breast irradiation therapy is required, breastfeeding can continue from the contralateral breast. In some settings, it may be reasonable and in fact preferred to defer resumption of systemic therapy to allow for postpartum healing during which time breastfeeding may be pursued for a period.

In utero chemotherapy exposure before 12 weeks of gestation has been associated with an increased risk of congenital malformations, due to organogenesis; however, later exposures are not linked to adverse long-term physical, cognitive, and behavioral development. Subtle differences have been observed in verbal IQ, visuospatial memory, and emotional regulation, but scores generally remain within normal limits and are more often attributed to prematurity than to chemotherapy itself, emphasizing the importance of avoiding preterm delivery when possible. Cardiac monitoring may be warranted in cases of anthracycline exposure, especially idarubicin, which has been associated with neonatal cardiomyopathy. Similarly, children exposed to platinum-based agents, particularly cisplatin, may be at increased risk of hearing impairment, warranting auditory follow-up beyond standard newborn screening. Brainstem auditory evoked response testing is preferred over otoacoustic emissions screening at birth, as the latter may not detect hearing loss associated with platinum exposure. Despite the reassuring follow-up data, interpretation is limited by small sample sizes, heterogeneous study designs, and the underrepresentation of early gestational exposures. Moreover, data on newer oncologic agents are limited and there is also a lack of long-term follow-up into adulthood, particularly regarding fertility outcomes.

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Therefore, continued long-term surveillance of exposed offspring is recommended.

There is an increased rate of depression and anxiety in patients with pregnancy-associated cancers, with risk factors for long-term psychological distress including preterm birth, caesarean delivery, breastfeeding difficulties, fertility challenges, decisions about pregnancy termination, disease recurrence, and postpartum surgery.[447,467] Patients who have cancer during pregnancy often experience fears related to the baby's health, their own health, and their role as a parent. Concerns may include the potential impact of treatment on fetal development, future fertility, and long-term parenting capacity. Early engagement with psychological services and peer support groups, such as Hope for Two,[468] is crucial from the moment of diagnosis on.

Special attention and support should be given during the period when the patient is deciding whether to continue her pregnancy and understanding how that choice may influence her treatment options, as this phase is often accompanied by heightened anxiety, information overload, and complex ethical considerations. The dual identity of being both a patient and an expectant mother can create inner conflict because of tradeoffs or conflicts between maternal health and fetal safety. Health care teams must be attuned to this duality and communicate in an empathic, clear, and concise way, placing the patient at the center of care, while addressing concerns, misconceptions, and potential ethical or legal questions with sensitivity.

Care should be tailored to the unique needs of this predominantly young adult population, accounting for cultural and religious values around motherhood, abortion, illness, and medical interventions. Screening for distress, addressing social determinants, and planning for survivorship are central to holistic care. Coordination among oncology, obstetric, neonatology, complex family planning specialists, and mental health services is critical, particularly to support parenting concerns, infant bonding, partner and family stress, and the evolving psychosocial, developmental, and schooling needs of the child. Screening for distress, addressing intersecting social determinants of health, such as financial strain, housing insecurity, and access to childcare, and planning for survivorship are essential for improving quality of life and psychosocial outcomes. Trauma-informed and grief-sensitive care should also be available when needed.

DISCUSSION

Managing cancer during pregnancy demands a values-based approach that integrates ethical principles with each patient's personal circumstances. Upholding pregnant patients' autonomy requires the health care team to present comprehensive, unbiased information about all therapeutic options and their maternal and fetal risks[469] while embedding decision making within the patient's relational network.[470,471] In practice, this means actively involving partners and family members, who often serve as primary sources of support, while ensuring the patient retains final authority to accept or decline treatments.[472] The ASCO Ethical Guidance "Where Reproductive Health Care Is Limited by Law" reinforces these imperatives by affirming that core ethical duties, including patient autonomy, beneficence, nonmaleficence, and justice, must remain inviolable even when legal constraints limit local clinical options.[13] It calls on institutions to provide clear, unbiased counseling on all standard-of-care treatments including termination, to protect patient confidentiality by minimizing nonessential documentation, and to establish safe transfer and referral mechanisms, potentially across state lines, to ensure uninterrupted access to reproductive services.[13]

Optimal management also relies on a multidisciplinary team approach, uniting medical, surgical, and radiation oncologists with maternal-fetal medicine specialists, neonatologists, genetic counselors, primary care clinicians, nurses, and psychosocial support providers. This collaborative model facilitates holistic care planning, where each specialist contributes expertise on timing, sequencing, and safety of interventions. Treatment plans must be individualized according to gestational age, cancer type and stage, and the pregnant patient's personal goals, whether that is prioritizing fetal maturity, maternal survival, or fertility preservation, ensuring that both maternal and fetal outcomes are optimized.[472,473]

Ethical care also hinges on balancing maternal beneficence with fetal welfare under conditions of clinical uncertainty. When robust safety data are lacking, particularly for novel chemotherapeutic agents or targeted therapies, clinicians must weigh potential patient benefit against the principle of "first, do no harm" to her fetus.[473] Emerging guidance underscores that, in most scenarios, maternal and fetal interests converge, and prioritizing maternal health often yields the best overall outcome.[472] Nonetheless, systemic justice considerations arise when legal restrictions on reproductive health care constrain treatment choices or trial enrollment,[13] which may result in maternal harm, as well as exacerbation of inequities, particularly for marginalized patients. To address these challenges, clinicians should establish clear referral pathways and advocacy mechanisms to navigate legal barriers,[348] ensure transparent institutional policies, strengthen informed-consent processes, including fertility preservation and contraceptive counseling, and implement robust privacy safeguards and clinician support systems to sustain ethically sound, equitable care for all pregnant patients with cancer.[13]

LIMITATIONS OF THE RESEARCH AND FUTURE RESEARCH

The evidence base informing the management of pregnant patients with cancer remains limited by several key methodological and clinical constraints. Most data come from nonclinical data (ie, animal data available in the drug label

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such embryo-fetal and fertility toxicology studies), retrospective observational studies, small case series, or case reports, leading to inherent risks of selection bias, confounding, and incomplete outcome data. There is a lack of randomized controlled trials, primarily due to ethical considerations, which limits the strength of causal inferences. Heterogeneity across studies, in terms of cancer types, treatment regimens, timing of exposure during gestation, and outcome reporting, further complicates data synthesis and comparison. Long-term fetal and child outcomes are rarely reported, and existing follow-up is often limited to neonatal end points. Additionally, publication bias may skew available evidence toward positive outcomes. These limitations collectively reduce the overall certainty of the evidence and underscore the need for cautious interpretation and individualized clinical decision making guided by multidisciplinary expertise.

Future research should prioritize the systematic inclusion of pregnant patients with cancer through ethically designed clinical trials or parallel registries to ensure evidence-based care. While traditional randomized trials may remain challenging, adaptive or observational trial designs could offer pathways for safer inclusion. Prospective registries, such as those led by the INCIP[464] and the Cancer and Pregnancy registry (ClinicalTrials.gov identifier: NCT02749474), play a critical role in gathering long-term maternal, fetal, and child outcome data, and should be expanded and harmonized globally. Additionally, research into emerging cancer therapies with lower teratogenic potential, as well as safer radiation techniques, is essential to broaden therapeutic options during pregnancy. Dedicated pharmacokinetic studies (human and animal) are also urgently needed to understand how pregnancy affects drug absorption, distribution, metabolism, and excretion, enabling clinicians to refine dosing strategies and maximize both maternal efficacy and fetal safety. Together, these efforts will strengthen the evidence base and support the development of more precise, individualized guidelines for this complex patient population.

PATIENT AND CLINICIAN COMMUNICATION

Effective communication between clinicians and pregnant patients diagnosed with cancer is critical to ensuring informed, values-based decision making and minimizing emotional distress. At the outset, clinicians should assess each patient's baseline understanding, information preferences, and emotional state, adapting explanations of diagnosis and treatment options to a clear, nontechnical level. Empathetic engagement helps to validate patient concerns while maintaining a supportive dialogue. Information about the timing, safety, and potential impacts of chemotherapy, surgery, or radiation should be conveyed in small, digestible segments, clearly delineating benefits for maternal survival alongside potential fetal risks by trimester, and supplemented with simple diagrams or decision aids when possible.

Shared decision making underpins this dialogue: clinicians present all medically appropriate options alongside their known benefits, risks, and uncertainties, while patients articulate personal goals, whether to prioritize continuing and prolonging pregnancy, preserving fertility, or optimizing maternal health. Integrating a multidisciplinary team, including obstetricians, maternal-fetal medicine specialists, complex family planning obstetricians, genetic counselors, nurses, and psychosocial providers, ensures consistent messaging and comprehensive care planning. Regular team case conferences and dedicated patient navigators further streamline communication, coordinate appointments, and connect families with peer support networks. Throughout treatment and into survivorship, clinicians should revisit emerging concerns, such as symptom management, potential late effects on child development, and breastfeeding safety, and proactively outline long-term follow-up schedules for both mother and child.

Financial and practical considerations are integral to patient-clinician discussions. Early engagement of social workers and financial counselors can clarify insurance coverage for cancer treatment during pregnancy, identify assistance programs, and address the added burden of frequent medical visits. Psychosocial support, through counseling, support groups, or patient navigator programs, mitigates anxiety, reduces decisional conflict, and fosters resilience. Finally, survivorship planning should begin before treatment completion, covering fertility preservation options, postpartum health monitoring, and developmental surveillance for the child, thereby ensuring a seamless transition from active cancer management to long-term wellness care.

For recommendations and strategies to optimize patient-clinician communication, see Patient-Clinician Communication: ASCO Consensus Guideline.[462]

PATIENT ACCESS CONSIDERATIONS

Not all patients have consistent access to the resources needed to benefit from ASCO's expert recommendations on best practices for prevention, screening, palliative and supportive care, and disease management of cancer. Access to comprehensive cancer care, including surgery, systemic therapies, and radiation, remains unevenly distributed across the United States, with both geographic and sociodemographic factors compounding barriers for pregnant patients. Based on US Cancer Statistics and National Center for Health Statistics data, an estimated 3,672 pregnant individuals are diagnosed with cancer each year, of whom 30.9% have breast cancer and 14.7% have female genital

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DISCUSSION POINTS BETWEEN PATIENTS AND CLINICIANS

Goals of Care
- If the patient chooses to continue her pregnancy, clarify maternal and fetal priorities, including desired pregnancy duration and acceptable trade-offs between treatment intensity and gestational timing.

Risks and Benefits of Therapeutic Options
- Compare safety profiles of chemotherapy regimens by trimester, timing of surgical interventions, and approaches to minimize fetal radiation exposure.
- Use plain-language summaries and simple visuals to illustrate potential maternal outcomes, risks of preterm birth, and developmental considerations.

Comorbidities
- Evaluate how existing conditions (eg, hypertension, diabetes, cardiac disease) may influence treatment selection, dosing schedules, and monitoring protocols.
- Coordinate care with relevant specialists to optimize both oncologic and obstetric management.

Biomarker and Genetic Testing
- Explain how tumor profiling may inform targeted therapies, potential postpartum treatment plans, and implications for familial genetic risk.
- Discuss timing of tests relative to pregnancy and how results may affect eligibility for clinical trials.

Clinical Trials
- Present available research studies, key inclusion and exclusion criteria, and potential benefits of experimental therapies balanced against unknown fetal risks.

Common Concerns
- Treatment burden and symptom management: Establish symptom tracking protocols, previsit checklists, and strategies for managing nausea, fatigue, or pain.
- Psychosocial needs: Screen for anxiety, depression, and caregiver stress; refer to mental health professionals and peer support groups.
- Financial and insurance issues: Review coverage for cancer care during pregnancy, identify financial aid resources, and involve social work early to navigate paperwork.

Survivorship Planning
- Plan for postpartum concerns, including breastfeeding safety, lactation support, and coordination of pediatric follow-up for developmental monitoring.
- Establish a long-term care schedule integrating oncology surveillance, obstetric care, and primary care, with clear points of contact for emerging health issues.

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tract malignancies.[474] Yet roughly two thirds of rural counties have no oncologist,[475] and 36% of US counties qualify as maternity-care deserts without any obstetric services,[476] forcing many patients to travel prohibitive distances for both prenatal and cancer-directed treatments.

Insurance coverage gaps exacerbate these challenges. Although most pregnant patients carry some form of health insurance, nearly one third of women age 19-44 years are underinsured, facing high deductibles and cost-sharing that frequently delay or preclude essential care such as imaging, biomarker testing, surgery, or timely initiation of chemotherapy, while an estimated 25 million US residents remain uninsured.[477] Among those with cancer during pregnancy, retrospective claims-based analyses have demonstrated that patients insured through Medicaid experience pregnancy loss more frequently, and live birth less frequently, than their commercially insured counterparts (31.6% *v* 25.8% and 59.7% *v* 67.1%, respectively), underscoring how insurance status deepens disparities in maternal and fetal outcomes.[478]

Intersectional inequities in access further disadvantage racial and ethnic minorities. Hispanic women of reproductive age living in states with complete abortion bans bear the highest incidence of cervical cancer, 8.29 per 100,000 in Texas versus 4.17 per 100,000 among White women in California, and would face an estimated 250-mile increase

in travel to the nearest abortion facility, effectively obstructing timely interventions that in some cases require treatment-related early delivery or termination.[474] Similarly, Black women experience longer delays between abnormal screening and follow-up diagnostics, presenting at more advanced stages and suffering higher mortality rates from both breast and gynecologic malignancies.[477]

In the United States, many patients remain unable to reap the benefits of innovative prevention and early detection programs, biomarker testing, and new cancer therapies due to challenges including lack of transportation, stable housing, adequate insurance coverage, food insecurity, health literacy, proximity to a dedicated cancer center, and cost of treatment and other services.[479] Additionally, some populations experience stigma along with barriers to cancer screening, prevention, and treatment that contribute to these cancer disparities.[480]

Further, geographic disparities can also impact the quality-of-care patients receive. Rural patients are more likely to have worse survivorship outcomes and experience higher mortality rates compared with nonrural patients. This can be attributed, in part, to a lower density of specialists and dedicated cancer centers, as only 21% of nonmetropolitan counties in the United States have one or more practicing oncologists.[481]

Taken together, these geographic maldistribution, insurance inadequacy, and systemic inequities create significant barriers to equitable, guideline-concordant care for pregnant patients with cancer. Recognition of these patient-access considerations is critical for the design of future interventions, whether through expanded insurance benefits that reduce underinsurance, colocation of obstetric and oncology services, or tele-oncology and patient navigation programs, to ensure that all pregnant individuals receive timely surgery, systemic therapy, and radiation as indicated by best practice guidelines.

MULTIPLE CHRONIC CONDITIONS

Creating evidence-based recommendations to inform treatment of patients with additional chronic conditions, a situation in which the patient may have two or more such conditions—referred to as multiple chronic conditions (MCC)—is challenging. Patients with MCC are a complex and heterogeneous population, making it difficult to account for all of the possible permutations to develop specific recommendations for care. In addition, the best available evidence for treating index conditions, such as cancer, is often from clinical trials whose study selection criteria may exclude these patients to avoid potential interaction effects or confounding of results associated with MCC. As a result, the reliability of outcome data from these studies may be limited, thereby creating constraints for expert groups to make recommendations for care in this heterogeneous patient population.

As many patients for whom guideline recommendations apply present with MCC, any treatment plan needs to take into account the complexity and uncertainty created by the presence of MCC and highlights the importance of shared decision making regarding guideline use and implementation. Therefore, in consideration of recommended care for the target index condition, clinicians should review all other chronic conditions present in the patient and take those conditions into account when formulating the treatment and follow-up plan.

In light of these considerations, practice guidelines should provide information on how to apply the recommendations for patients with MCC, perhaps as a qualifying statement for recommended care. This may mean that some or all of the recommended care options are modified or not applied, as determined by best practice in consideration of any MCC.

GUIDELINE IMPLEMENTATION

ASCO guidelines are developed for implementation across health settings. Each ASCO guideline includes a community oncologist member on the panel. The additional role of this community oncologist member on the guideline panel is to assess the suitability of the recommendations for implementation in the community setting, but also to identify any other barrier to implementation a reader should be aware of. Barriers to implementation include the need to increase awareness of the guideline recommendations among front-line practitioners and survivors of cancer and caregivers, and also to provide adequate services in the face of limited resources. The guideline recommendations table and accompanying tools (available at www.asco.org/survivorship-guidelines) were designed to facilitate implementation of recommendations. This guideline will be distributed widely. ASCO guidelines are posted on the ASCO website and most often published in the *Journal of Clinical Oncology*.

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate.

ADDITIONAL RESOURCES

For current information, including selected updates, supplements, and clinical tools and resources, visit www.asco.org/survivorship-guidelines. The Data Supplement (online only) for this guideline includes the literature search strategy, QUORUM diagram, and implementability review. Guideline recommendations and algorithms are also available in the free ASCO Guidelines app (available for download in the Apple App Store and Google Play Store). Listen to key recommendations and insights from panel members on the ASCO Guidelines podcast. The Methodology Manual (available at www.asco.org/guideline-methodology)

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provides additional information about the methods used to develop this guideline. Patient information is available at www.cancer.org.

ASCO welcomes your comments on this guideline, including implementation challenges, new evidence, and how this guideline impacts you. To provide feedback, contact us at guidelines@asco.org. Comments may be incorporated into a future guideline update. To submit new evidence or suggest a topic for guideline development, complete the form available at www.asco.org/guidelines.

INCLUSIVE LANGUAGE

ASCO is committed to promoting the health and well-being of all patients. ASCO guidelines are intended to apply to, and be discussed clearly and compassionately with, all patients. For this reason, guideline authors use appropriately inclusive language. In instances in which the guideline draws upon data based on research in a specified population (eg, studies regarding women with ovarian cancer), the guideline authors describe the characteristics and results of the research as reported.

RELATED ASCO GUIDELINES

- Patient-Clinician Communication[462] (https://ascopubs.org/doi/10.1200/JCO.2017.75.2311)
- Sentinel Lymph Node Biopsy in Early-Stage Breast Cancer[482] (https://ascopubs.org/doi/10.1200/JCO-25-00099)
- Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer[483] (https://ascopubs.org/doi/10.1200/JCO.23.00294)
- Antiemetics[484] (https://ascopubs.org/doi/10.1200/JCO.20.01296)
- Fertility Preservation in People With Cancer[485] (https://ascopubs.org/doi/10.1200/JCO-24-02782)
- Management of Anxiety and Depression in Adult Survivors of Cancer[456] (https://ascopubs.org/doi/10.1200/JCO.23.00293)
- Palliative Care for Patients With Cancer[486] (https://ascopubs.org/doi/10.1200/JCO.24.00542)

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AFFILIATIONS

[1]Perelman School of Medicine of the University of Pennsylvania, Philadelphia, PA
[2]American Society of Clinical Oncology, Alexandria, VA
[3]University Hospitals Leuven, Leuven, Belgium
[4]Cooper University Health Care, Camden, NJ
[5]University of North Carolina, Chapel Hill, NC
[6]University of Colorado, Denver, CO
[7]Oncology Nursing Society, Pittsburgh, PA
[8]Tufts University School of Medicine, Boston, MA
[9]McGill University, Montréal, QC, Canada
[10]St Jude Children's Research Hospital, Memphis, TN
[11]GRASP Cancer, Baltimore, MD
[12]Medical College of Wisconsin, Milwaukee, WI
[13]Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD
[14]Messino Cancer Centers, Asheville, NC
[15]University of Texas MD Anderson Cancer Center, Houston, TX
[16]Department of Oncological Sciences, Florida International University, Miami, FL
[17]Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL
[18]University of California San Francisco, San Francisco, CA
[19]The University of Edinburgh, Edinburgh, Scotland
[20]Feinberg School of Medicine, Northwestern University, Chicago, IL
[21]Mayo Clinic, Rochester, MN
[22]Dana-Farber Cancer Institute, Boston, MA

CORRESPONDING AUTHOR

American Society of Clinical Oncology; e-mail: guidelines@asco.org.

DISCLAIMER

The views expressed in this manuscript are those of the authors and do not reflect the views of the US Food and Drug Administration, the Department of Health and Human Services, or the US government.

EDITOR'S NOTE

This ASCO Clinical Practice Guideline provides recommendations, with comprehensive review and analyses of the relevant literature for each recommendation. Additional information, including a supplement with additional evidence tables, slide sets, clinical tools and resources, and links to patient information at www.cancer.org, is available at www.asco.org/survivorship-guidelines

EQUAL CONTRIBUTION

A.W.L. and A.H.P. were Expert Panel Cochairs.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTIONS

Conception and design: Alison W. Loren, Christina Lacchetti, Lisa Carey, Don Dizon, Melissa Henry, Melissa Hudson, Erika Peterson, Tatiana Prowell, Rachel Raab, Jane E. Rogers, Hina Saeed, Mikkael A. Sekeres, Jolyn Taylor, W. Hamish Wallace, Katie L. Watson, Siddhartha Yadav, Ann H. Partridge
Provision of study materials or patients: Jane E. Rogers
Collection and assembly of data: Christina Lacchetti, Elyce Cardonick, Don Dizon, Melissa Henry, Tatiana Prowell, Rachel Raab, Jane E. Rogers, Hina Saeed, Jolyn Taylor, Katherine Van Loon, W. Hamish Wallace, Siddhartha Yadav, Ann H. Partridge
Data analysis and interpretation: Alison W. Loren, Christina Lacchetti, Frédéric Amant, Lisa Carey, Nicole Christian, Caroline Clark, Don Dizon,

Melissa Henry, Melissa Hudson, Julia Maués, Erika Peterson, Tatiana Prowell, Rachel Raab, Jane E. Rogers, Hina Saeed, Mikkael A. Sekeres, Jolyn Taylor, Katherine Van Loon, W. Hamish Wallace, Katie L. Watson, Siddhartha Yadav, Ann H. Partridge
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Management of Cancer During Pregnancy: ASCO Guideline

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Alison W. Loren
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Caroline Clark
Consulting or Advisory Role: Pfizer (Inst), American Hospital Formulary Service (Inst)

Don Dizon
Stock and Other Ownership Interests: Midi, Doximity
Honoraria: UpToDate, American Cancer Society
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Research Funding: Bristol Myers Squibb (Inst)
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Melissa Hudson
Employment: Methodist Hospital (I)
Consulting or Advisory Role: Princess Máxima Center, VIVA Foundation Singapore

Jane E. Rogers
Consulting or Advisory Role: ProLynx, National Community Oncology Dispensing Association (NCODA)

Mikkael A. Sekeres
This author is an Associate Editor for *Journal of Clinical Oncology*. Journal policy recused the author from having any role in the peer review of this manuscript.
Consulting or Advisory Role: Kurome Therapeutics, Bristol Myers Squibb/Celgene, Agios, AstraZeneca, Geron
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Katherine Van Loon
Research Funding: Natera

Siddhartha Yadav
Consulting or Advisory Role: AstraZeneca (Inst)
Research Funding: REPARE Therapeutics (Inst), AstraZeneca (Inst), Exelixis (Inst), 858 Therapeutics (Inst)
Open Payments Link: https://openpaymentsdata.cms.gov/physician/1025796

Ann H. Partridge
Patents, Royalties, Other Intellectual Property: Wolters Kluwer-royalties for authorship of UpToDate
Open Payments Link: https://openpaymentsdata.cms.gov/physician/835197

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APPENDIX 2. GUIDELINE AND CONFLICTS OF INTEREST

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TABLE A1. Management of Cancer During Pregnancy Guideline Expert Panel Membership

Name	Affiliation	Role or Area of Expertise
Alison Loren, MD, MSCE (co-chair)	Perelman School of Medicine of the University of Pennsylvania, Philadelphia, PA	Hematology/Medical Oncology
Ann Partridge, MD, MPH (co-chair)	Dana-Farber Cancer Institute, Boston, MA	Breast Medical Oncology
Frédéric Amant, MD, PhD	University Hospitals Leuven, Leuven, Belgium	OB/GYN
Elyce Cardonick, MD, FACOG	Cooper University Health Care, Camden, NJ	Maternal Fetal Medicine
Lisa Carey, MD	University of North Carolina, Chapel Hill, NC	Breast Medical Oncology
Nicole Christian, MD	University of Colorado, Denver, CO	Breast Surgical Oncology
Caroline Clark, MSN, APRN, OCN	Oncology Nursing Society, Pittsburgh, PA	Oncology Nursing Society Representative
Don Dizon, MD	Tufts University School of Medicine, Boston, MA	GYN Medical Oncology
Melissa Henry, PhD	McGill University, Montréal, Québec, Canada	Psychosocial Oncology
Melissa Hudson, MD	St Jude Children's Research Hospital, Memphis, TN	AYA Oncology
Julia Maués, MA	GRASP Cancer, Baltimore, MD	Patient Representative
Erika Peterson, MD	Medical College of Wisconsin, Milwaukee, WI	Maternal Fetal Medicine
Tatiana Prowell, MD	Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD	Medical Oncology
Rachel Raab, MD	Messino Cancer Centers, Asheville, NC	Community Oncology
Jane E. Rogers, PharmD, BCOP	University of Texas MD Anderson Cancer Center, Houston, TX	Oncology Pharmacy
Hina Saeed, MD	Department of Oncological Sciences, Florida International University, Miami, FL	Radiation Oncology ASTRO Representative
Mikkael A. Sekeres, MD	Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL	Hematology/Medical Oncology
Jolyn Taylor, MD	MD Anderson Cancer Center, Houston, TX	GYN Surgical Oncology
Katherine Van Loon, MD, MPH	University of California San Francisco, San Francisco, CA	GI Medical Oncology
W. Hamish Wallace, MD	The University of Edinburgh, Edinburgh, Scotland	Pediatric Oncology
Katie L. Watson, JD	Feinberg School of Medicine, Northwestern University, Chicago, IL	Ethics
Siddhartha Yadav, MD	Mayo Clinic, Rochester, MN	Breast/GYN Medical Oncology
Eias Zahalka, PhD, MBA	—	Toxicology/Pharmacology
Christina Lacchetti, MHSc	American Society of Clinical Oncology (ASCO), Alexandria, VA	ASCO Practice Guideline Staff (Health Research Methods)

NOTE. The views expressed in the manuscript are those of the authors and do not reflect the views of the US Food and Drug Administration, the Department of Health and Human Services, or the US government.

Abbreviations: ASTRO, American Society for Radiation Oncology; AYA, adolescent and young adult; GYN, gynecologic; OB/GYN, obstetrician-gynecologist.

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TABLE A2. Evidence Quality and Recommendation Rating Definitions

Term	Definition
Evidence quality	
High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect
Strength of recommendation	
Strong	In recommendations for an intervention, the desirable effects of an intervention outweigh its undesirable effects In recommendations against an intervention, the undesirable effects of an intervention outweigh its desirable effects All or almost all informed people would make the recommended choice for or against an intervention
Conditional	In recommendations for an intervention, the desirable effects probably outweigh the undesirable effects, but appreciable uncertainty exists In recommendations against an intervention, the undesirable effects probably outweigh the desirable effects, but appreciable uncertainty exists Most informed people would choose the recommended course of action, but a substantial number would not

NOTE. GRADE Handbook, Schünemann et al.[487]

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